The Role of Fuel Cells in Advancing Pharmaceutical Technologies: Applications and Future Perspectives

[1]Hanan Saleh Almasmary, [2]Hamad Hussein Masoud Al Mansour, [3]Misfer Hadi ALSalom, [4]Safiyah Mohammad Saeed Alghamdi, [5]Munayfah Mohammed Munawir Alanazi, [6]Maha Abdulrahman Ibrahim Alowais, [7]Fahda Ahmad Hatab Al Anazi, [8]Tahani Saad Alamri, [9]Reem Abdullah Alanazi,

[1]Pharmacist, Moh, Riyadh
[2]Pharmacist Technician, Al Thaybah Clinic, Najran
[3]Clinical pharmacy, Habouna General Hospital, Najran
[4]Pharmacist, Alymama Hospital, Riyadh
[5]Pharmacist, Alyamamah hospital, Riyadh
[6]Pharmacist, Alyamamah hospital, Riyadh
[7]Pharmacist, Alyamamah hospital, Riyadh
[8]Pharmacist, Alyamamah hospital, Riyadh
[9]Pharmacist, Alyammamah hospital, Riyadh

1. Introduction

The pharmaceutical industry is vital for public health and modern life. However, drug misadventures, especially during drug development, create significant costs for the pharmaceutical sector. With rising energy costs and environmental concerns, drug manufacturers must consider energy use and carbon impact. Fuel cells, which convert a fuel's chemical energy directly into electrical energy, promise efficient on-site energy production and zero emission alternatives to burning fossil fuels. Their adoption relies on a balance of upfront costs and long-term benefits. This essay discusses fuel cells' current and potential applications in the pharmaceutical industry, where energy use is often hidden.

A fuel cell system transforms the chemical energy of fuel into electricity, with water and heat as byproducts, and has five fundamental components: the fuel cell stack, a fuel processor, power conditioning, and two auxiliary subsystems (fuel supply and temperature control). Fuel cells are high-efficiency generators used in various industrial applications. There are several variations of fuel cells beyond the most common hydrogen fuel cells, such as phosphoric acid, sodium hydroxide (alkali), and solid oxide fuel cells. As portable energy sources and electricity generators for stationary applications, fuel cells are deemed viable alternatives to batteries and internal combustion engines. Phosphoric acid fuel cells are often preferred in stationary applications due to their high tolerance to carbon monoxide impurities and ability to use ethanol and natural gas fuels (K. Niakolas et al., 2016).

2. Fundamentals of Fuel Cells

Fuel cells are electrochemical devices that convert the chemical energy of a fuel directly into electrical energy through a series of oxidation and reduction reactions. Most commonly used fuel for fuel cells is hydrogen, but other options, like hydrocarbons and biofuels, also exist. Fuel cells operate on the basis of electrochemical reactions and consume reactants from an external source (K. Niakolas et al., 2016). They are favorable alternatives to conventional electricity generation methods for small-scale applications. Considering the nature of applied fuel and the type of electrolyte, there are five widely discussed types of fuel cells: Polymer Electrolyte Membrane Fuel Cells (PEMFC), Direct Methanol Fuel Cells (DMFC), Phosphoric Acid Fuel Cells (PAFC), Molten Carbonate Fuel Cells (MCFC), and Solid Oxide Fuel Cells (SOFC). Among them, PEMFC and DMFC are low-temperature fuel cells, while PAFC, MCFC, and SOFC operate at high temperatures. Fuel cells can also be classified based on their operating temperature, efficiency, applications, and costs. This chapter mainly focuses on low-temperature fuel cells, as they are the most relevant for the pharmaceutical industry. The basic principle of operation of a fuel cell is that for two or more reactants that would like to form a compound, an electrochemical potential exists between the ionic forms of those reactants (Reifsnider et al., 2005). In a fuel cell, the reactants, oxygen and hydrogen ions, are separated by an electrolyte, so an electrical charge develops across the cell. If the electrolyte is chosen so that ions of one of the reactant species are conducted through that layer, then an electrical circuit can be completed by connecting the outside layers of material of the cell, and the electrical potential will provide power to the external electrical load. In simple terms, fuel cells are devices that convert chemical energy into electrical energy. They have several advantages over conventional energy conversion technologies, such as having no moving parts, scalability, tolerance to fuel impurities, and modularity, and being suitable for distributed energy conversion systems.

2.1. Types of Fuel Cells

Fuel cells can be categorized based on the nature of the electrolyte used. There are five types of fuel cells, namely Proton Exchange Membrane Fuel Cells (PEMFC), Phosphoric Acid Fuel Cells (PAFC), Alkaline Fuel Cells (AFC), Molten Carbonate Fuel Cells (MCFC), and Solid Oxide Fuel Cells (SOFC). Each of these types has its own unique features and functionalities. However, all fuel cells have basic components like the anode section, cathode section, electrolyte, and external load (Yue, 2019). During operation, the fuel cell requires continuous supplies of fuel and oxidizer, as well as a mechanism for elimination of byproducts. The extent of chemical reaction is characterized by current density which is defined as the current per unit working area. Each type of fuel cell has different performance characteristics. There are various types of fuel cells defined based on the electrolyte used. Out of these five types, SOFC and PEMFC are the most promising fuel cell technologies. SOFC uses a solid ceramic electrolyte and operates at 650–1000 ˚C temperature range. The advantage of SOFC is its ability to use a variety of fuels. However, the disadvantage is the long start-up time and requirement of huge and expensive high-temperature tolerant materials for interconnect and seals. Whereas PEMFC uses a polymer electrolyte that conducts only protons and operates below 100 ˚C. The advantages of PEMFC are its low operating temperature and quick start-up time. But it uses expensive noble metal catalysts and needs high-purity hydrogen fuel. Fuel cells are electrochemical devices that convert chemical energy into electrical energy and heat through a series of oxidation and reduction reactions. Fuel cells are classified into five major types namely, Proton Exchange Membrane Fuel Cells (PEMFC), Phosphoric Acid Fuel Cells (PAFC), Alkaline Fuel Cells (AFC), Molten Carbonate Fuel Cells (MCFC), and Solid Oxide Fuel Cells (SOFC). Each type of fuel cell differs from one another based on the electrolyte used and the operating temperature. In general, low temperature fuel cells (operating below 200 ˚C) suffer from the Carbon Monoxide poisoning of the catalysts and Membrane Electrode Assemblies (MEA) dehydration. PEMFC has a polymer electrolyte that conducts only protons and the fuel is usually hydrogen. Heat and water are the byproducts of these fuel cells.

2.2. Operating Principles

Fuel cells harness the chemical energy of fuels through electrochemical reactions to produce electricity. The device for generating power from fuel cells is called a fuel cell. Fuel cells generate electrical energy by means of reversible electrochemical reactions using chemical fuels and oxidants. The basic arrangement of a fuel cell includes an anode, a cathode, and an electrolyte located between the two electrodes. The fuel cell uses hydrogen as fuel and oxygen (or air) as an oxidizer, producing electricity, water, and heat as byproducts (Reifsnider et al., 2005). During operation, hydrogen gas (H2) enters the anode side and is converted to protons (H+) and electrons (e−) through an electrocatalytic reaction. Protons migrate to the cathode side through the electrolyte, while electrons travel through the external circuit, generating an electric power output. At the cathode side of the fuel cell, oxygen from the air combines with protons and electrons to generate water.

Fuel cells have a variety of applications, including stationary, portable, and transport applications. Fuel cells are being commercially developed for use in vehicles, including automotive, bus, rail, and marine applications. There are existing fuel cell cars from major automobile manufacturers, including a growing number of hydrogen refueling stations. Densely populated urban areas are seeing fuel cell electric buses deployed commercially in large fleets. Long-term tests of fuel cell light-duty trucks are being carried out in tough refuse collection conditions. The benefits of fuel cells over traditional combustion engines include being nearly silent with no noxious tailpipe emissions or solid particle emissions (Ofualagba et al., 2012). Fuel cells can also be applied to pharmaceutical technology in providing clean energy for sensitive processes. Ubiquitous, miniaturized fuel cells may lead to novel, portable applications in pharmaceutical technology. The basic operating principles of fuel cells are described here to provide a foundation for appreciating their applications. In addition, methods for modeling fuel cell dynamic and steady-state behavior are briefly reviewed to facilitate understanding of the efficiency improvements discussed.

3. Current Applications of Fuel Cells in Pharmaceutical Technologies

Clinical and pharmacy technologies have made huge strides in recent years, mostly due to the advancement of drug delivery systems and biosensors. Drug delivery systems have evolved from a relatively passive diffusion-transport-based design to a more active one, where smart drug delivery systems can respond to physiological changes and precisely control the rate, duration, and site of drug delivery. The sensing/monitoring devices in patient care have also transformed from a laboratory-based, time-consuming, and invasive approach to a more proactive point-of-care (POC) monitoring system, which is often non-invasive, can provide immediate results, and minimizes the need for patient interactions with clinical facilities (K. Niakolas et al., 2016).

Over the past couple of decades, fuel cells technology has been intensively developed and used in various applications from automobiles to small portable electronic devices. Fuel cells have also been explored and used within the pharmaceutical technologies, including drug delivery systems and sensing/monitoring devices. This section reviews the current applications of fuel cells in pharmaceutical technologies, focusing on the existing technological implementations rather than basic research or theoretical analysis. The intent is to introduce the readers to where the fuel cell technology currently stands within the pharmaceutical industry, with some example applications from recent literature. It is hoped that this would stimulate more interests in the biomedical/pharmaceutical research community in exploring fuel cells technology as a means to improve, or even revolutionize, the current pharmaceutical practices.

3.1. Drug Delivery Systems

In recent years, fuel cell technology has found a new niche in pharmaceuticals and drug delivery systems. As traditional methods usually rely on passive diffusion through membranes, new technologies are being developed to actively control the drug release. Fuel cells have emerged as an innovative way to apply the active concept to drug delivery systems, having been previously utilized to develop self-powered or battery-free mechanisms in various applications. The integration of miniature fuel cells into drug delivery systems opens up new possibilities to address existing challenges. Fuel cell-based drug delivery systems can switch from passive to active mode by simply integrating a redox fuel cell, enabling the controlled mode of drug release and improving the treatment efficacy (Ma et al., 2022). This section will focus on the specific applications of fuel cells in drug delivery systems.

Passive drug delivery systems cascade the bioactive agents diffusion through membranes, and usually only one drug is contained in a matrix. As a result, the peak concentration of the drug is achieved shortly after the administration, and the drug concentration gradually decreases over time. For many diseases, this is not optimal. In some cases, a drug is needed continuously over a long period; in others, multiple administrations are required because the concentration drops below the effective level or to prevent the resurgence of the disease. Moreover, the drug concentration needs to be kept within a certain range, as excess concentrations can cause toxicity and side effects. This motivated the development of drug delivery systems that can better mimic natural secretion, maintain optimal concentration of drugs over time, and control the release profile. Normally, a combination of different approaches such as new materials, devices, and methods is used to achieve this goal. However, one general strategy is to switch drug delivery systems from passive to active mode, where the drug release can be accurately controlled. In the active mode, a driving system is often required, which can be driven mechanically, magnetically, electrochemically, or by lasers. The biggest advantage of the active mode is that drug release can be accurately controlled. Recently, more attention has been paid to the application of new technologies to drive drug delivery. (Geraili et al., 2021)(Liu et al., 2021)

3.2. Sensing and Monitoring Devices

The growing demand for real-time monitoring devices that can provide data on biological parameters has resulted in a number of novel sensing and monitoring devices being built using fuel cells. The recent progress in research and development of biomedical devices which can monitor important biological parameters in a reliable and efficient manner is reviewed here, focusing on those that use fuel cells as the main transducing element (Gonzalez-Solino & Di Lorenzo, 2018). These devices take advantage of the ability of fuel cells to transduce biological oxidation/reduction reactions into electrical current, and thus can be classified as biosensors, in which binding of an analyte to a biorecognition element causes a change in the fuel cell current. Some of these devices have already reached commercial status, while many others are still undergoing research and development.

Fuel cells have been successfully applied to the monitoring of a wide range of analytes, with particular emphasis on glucose monitoring during the past two decades. Other biomedical applications include the detection of disease biomarkers, as well as monitoring of neurotransmitters and pharmacological agents. Fuel cells used in fully implantable devices have been powered by bioluminescent bacteria and by enzymes coupled to nanoparticles that generate fuels such as H2 or different alcohols. However, most of the current research on fuel cell biomedical applications is focused on passive, macro, or miniaturized devices that run on physiological fluids such as sweat, saliva, tears, or blood. Such devices are especially well-suited for point-of-care, on-the-spot testing or for wearable or implantable devices that continuously monitor the state of health of the individual. They are an improvement on historical laboratory-based technologies that require samples to be taken from the patient and transported to central facilities for analysis, with a large turn-around time that can delay the initiation of treatment. Wearable versions of these devices can also be used to monitor individuals at risk in real-time, for example, in sports or occupational health applications.

4. Challenges and Future Directions

The need for fuel cells in pharmaceutical technologies is clear, but several challenges currently limit their pharmaceutical applicability. As evaluated above, fuel cells are not without limitations, and technological challenges remain in improving their performance and ensuring their stability. These limitations tend to become critical as the fuel cell solution is scaled to meet the pharmaceutical needs, as it must also be cost-effective. When considering the integration of novel technologies such as fuel cells into new pharmaceutical products and technologies, regulatory requirements must be adhered to. Any pharmaceutical product or technology must comply with current Good Manufacturing Practices (cGMP), which ensure the quality, safety, and efficacy of pharmaceutical products. Furthermore, specific to this literature review, regulations concerning the pharmaceutical applicability of the fuel cells must also be addressed (K. Niakolas et al., 2016). To fully appreciate the complexity of deploying fuel cell solutions in healthcare, it is crucial to understand what these regulations are and how they must be complied with. Although these regulatory hurdles are mostly generalized for pharmaceutical products and technologies, some pertain specifically to fuel cells. Nevertheless, ongoing research strives to overcome these challenges and advance fuel cell technology, paving the way for future fuel cell-based pharmaceutical products and technologies. Suggestions for possible future directions and innovations to fuel cell technologies to enhance efficiency or reduce production costs are also presented here. Most importantly, to advance pharmaceutical fuel cell technologies effectively, collaboration between the pharmaceutical sector and the fuel cell technology sector is needed. This will ensure that both the pharmaceutical needs and the current fuel cell limitations are sufficiently considered when selecting future research avenues.

4.1. Technological Limitations

This section addresses the limitations hindering fuel cell advancement in the pharmaceutical sector, focusing specifically on technological constraints. These limitations encompass issues affecting fuel cell performance, including low energy density, short operational lifespan, and specific power concerns. Additionally, challenges related to fuel storage in portable devices are discussed, along with considerations for fuel cell design and application that can alleviate some concerns. By narrowing the focus to technological limits, a clearer picture emerges of the reasons fuel cells struggle to find application in pharmaceuticals. Most limitations directly impact cost and scalability, with some requiring more basic research rather than advancement (K. Niakolas et al., 2016). As a result, developers are unable to adequately demonstrate the benefits of fuel cells to potential clients. An overview of the current state of fuel cell technology is presented, along with the most pressing limitations that require resolution for widespread adoption. Ongoing research efforts to address these constraints through innovative fuel cell designs or materials are highlighted, often exaggerating the shortcomings of competing technologies. While many limitations are clear, the need for improvement in fuel cell technology to meet the demands of the pharmaceutical industry is emphasized. There is no intention for this overview to be a literature review, as many cited works address only a subtopic of fuel cells. Instead, the objective is to provide an overall picture of the current state of the technology and the hurdles that must be resolved for future advancement.

4.2. Regulatory Hurdles

As fuel cell technology matures and finds more widespread implementation, there are several hurdles that need to be cleared before fuel cell applications are ready for pharmaceutical use. Generally speaking, the hurdles that need addressing are technical, economic, and regulatory issues. The following subsections will focus on the regulatory aspects of fuel cell integration. Regulations for medical technologies can be quite complex with numerous different regulations applying to different aspects of the technology. As most fuel cell applications are still experimental or proof-of-concept implementations, the regulatory compliancy for these systems is often lacking or has not yet been demonstrated. Some safety standards, like low voltage safety extra low voltage (LVSELV), are compatible with fuel cells systems, as additional risk mitigation layers may be added (KENZAOUI BLANKA et al., 2019). On the other hand, many safety standards, especially those for electro-mechanical systems, do not include fuel cell technology and as such cannot be effectively implemented on these systems. Approval and certification can be another substantial challenge, as it often requires extensive data collection on safety and efficacy, which in turn complicates adoption and increases costs. Most medical regulations focus on safety and efficacy, which for newer technologies necessitates extensive testing to comply with these regulations. This results in long timelines and cost increases, making it more difficult for start-ups, SMEs, and even some large companies to integrate new technologies. Furthermore, regulatory bodies are having ongoing discussions on how to assess new technologies, as the old paradigms often do not fit. This has resulted in some new avenues for assessment, but these are often still in their infancy. It is likely that many issues could be more effectively and more rapidly resolved through collaboration between stakeholders.

5. Conclusion

The substantial and innovative role of fuel cells in the advancement of emerging pharmaceutical technologies has been demonstrated. From drug delivery systems with unprecedented capacity, controllability, and biosecurity, to autonomous in-vivo diagnostic devices reliant on real-time biological energy harvesters, fuel cells promise to inspire revolutionary changes in healthcare systems. The current state of pharmaceutical technologies utilizing fuel cells has been highlighted, and a perspective on future development has been presented. Crucial considerations for future research directions – including technological challenges in materials, miniaturization, biocompatibility, and purely pharmaceutical-cell designs, as well as regulatory concerns spanning preclinical and clinical trials, safety, toxicity, and commercialization – have also been outlined. It is hoped that this emerging field will attract interest from researchers across diverse backgrounds, paving the way for further breakthroughs that will maximize the benefits of integrated pharmaceutical applications for social good (K. Niakolas et al., 2016).

In summary, fuel cells effectively convert chemical energy into electrical energy through electrochemical redox reactions, currently being utilized to generate portable power sources. Interest in applying fuel cells in the pharmaceutical field has been aroused due to their ability to construct bioenergy-regenerative drug delivery systems that directly utilize physiological bioenergy. Along with bioenergy-driven drug delivery systems, bioenergy-devices capable of in-vivo drug detection and real-time closed-loop drug release also have great potential in the pharmaceutical field. Although various proof-of-concept studies have been reported, there are still many challenges that need to be addressed before practical applications of fuel cells in the pharmaceutical field are realized.

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