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Review paper

Electroceutical: The rise of bioelectronic medicine

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ABSTRACT

Bioelectronic medicine encompasses technologies designed to modulate and exchange neural signaling patterns, achieving therapeutic effects by targeting specific organ functions. Bioelectronics technology facilitates real-time monitoring of treatment adherence and effectiveness, potentially leading to significant improvements in mortality and morbidity outcome. Bioelectronic medicines represent a distinct category of therapeutics, integrating both electronic devices and pharmacological agents. The components of bioelectronic medicine is Silicone-based Penetrating Electrodes, Polymer-based Electrodes, Polyimide. etc. By extension, it may be possible to target and modulate malfunctioning neural pathways using microelectrodes to correct these dysfunctions.

INTRODUCTION

Recent advancements in the bioelectronic field have been propelled by the development of more sophisticated devices and novel materials engineered at the nanoscale[1.]Bioelectronic medicine encompasses technologies designed to modulate and exchange neural signaling patterns, achieving therapeutic effects by targeting specific organ functions. The primary mechanism underlying bioelectronic medicine is the transfer of electrical signals, which facilitates the modulation of neural activity to produce desired therapeutic outcomes.[2]. Bioelectronic medicine represents a dynamic and advancing field where emerging understandings of the regulatory functions of the nervous system, combined with innovations in bioelectronic technologies, are leading to novel methodologies for disease diagnosis and therapeutic intervention [3]. Technological advancements significantly propel progress in scientific research and medical practice. There exists an urgent demand for more effective therapeutic interventions or curative strategies for a range of debilitating diseases and conditions. These include inflammatory and autoimmune disorders, obesity, diabetes mellitus, cardiovascular diseases, malignancies, neurodegenerative diseases, neuromuscular

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disorders, and spinal cord injuries [4].It utilizes electrical, magnetic, optical, and ultrasound pulses to modulate nerve activity, thereby influencing physiological functions as an alternative or adjunct to pharmacological treatments. Bioelectronic Medicine (BEM), employing neurotechnologies to interface with the nervous system, presents significant potential. Neurotechnologies represent one of the most rapidly expanding sectors within the medical device industry [5].It is an innovative therapeutic approach for disease management that employs electrical pulses as an alternative to pharmacological agents [6].Bioelectronics technology facilitates real-time monitoring of treatment adherence and effectiveness, potentially leading to significant improvements in mortality and morbidity outcomes. By providing continuous feedback and precise data on patient compliance and therapeutic impact, this technology could profoundly influence overall health outcomes and the management of chronic conditions [7]. Bioelectronic medicine represents an emerging field dedicated to devising therapeutic strategies that utilize electrical pulses rather than pharmacological agents. Advances in this domain enable the use of compact, implanted devices that generate and administer periodic digital stimuli to nerve bundles. These electrical impulses induce therapeutic effects comparable to those achieved through traditional drug therapies, with the duration of disease-modulating effects extending from hours todays [8].

History

Bio electrical medicine has a rich history that spans thosands of years..the discovery of bioelectricity by luigi galvani in 1791 marked the beginning of modern bio-electrical medicine.The development of electrotherapy in the 19th century led to the use of electrical stimulation to treat a range of conditions including pain, paralysis and muscle weakness. The development of pacemakers in the 1950s and 1960s revolutionized the treatment of heart rhythm disorders.The introduction of transcutaneous electrical nerve stimulation in 1970s provided a new approach to pain management. The development of implantable neurostimulators in the 1980s and 1990s expanded the range of conditions that could be treated with bio-electical medicine. Advances in technology including the development of more sophisticated electrodes and pulse generators have expanded the range of applications for bio-electrical medicine. The emergence of electroceuticals a newclass of bioelectical therapies that target specific nerves or neural circuits has opened up new possibilities for the treatment of a range conditions includding inflammatory disordersand neurological diseases [9-12].

Objectives

In Bioelectronic Medicine (BEM) therapy, the following objectives are essential:

- **Identification of Suitable Disease Targets:** Determining specific diseases that are amenable to Bioelectronic Medicine interventions is crucial for effective treatment application.
- **Modulating neural activity:** To modulate neural activity to treat a range of diseases and conditions like as chronic pain,parkinsons disease, epiilepsy.
- **Development of Investigative Devices:** To elucidate the underlying mechanisms of BEM therapy, there is a need for advanced investigative devices that can integrate with existing technologies to address and fill knowledge gaps.
- **Interdisciplinary Collaboration:** Effective BEM therapy requires coordinated efforts among biological, medical, and

computational disciplines to ensure comprehensive development and application.

- **Modeling Systemic Responses:** It is essential to develop biological, chemical, electrical, and mechanical models to accurately simulate and understand the physiological state of the body both in health and disease, facilitating a thorough comprehension of system behavior under pathological conditions [13].

Components

In bioelectronic medicine, interfaces are essential for accessing and interfacing with peripheral nerves. The components are

Electrodes:

- Silicone-based Penetrating Electrodes:
- Polymer-based Electrodes: Fine, time, life, and cuff electrode arrays
- Complementary Metal-Oxide-Semiconductor (CMOS)

Materials:

- Noble Metals and Alloys: Platinum, Platinum-Iridium, Gold
- Laser-Patterned Materials: Gold or Platinum-Iridium foil (12 micrometers), lithographically patterned thin films of gold or platinum (300 nm) on polyamide or polypropylene, thermally evaporated ultra-thin films (35 nm)

Polymers:

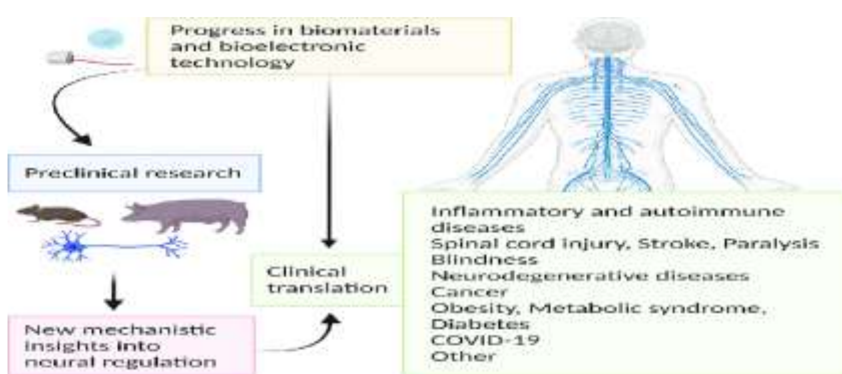
- Polyimide
- Parylene
- Polydimethylsiloxane (PDMS)
- Liquid Crystal Polymer SU-8 Photoresist Polyurethane
- Sheet or Film Materials: Polyimide

Optical Components:

- Light Emitting Diodes (LEDs): For optogenetic stimulation
- Receiving Elements: For wireless power transfer, including inductors, antennas, and ultrasonic transducers

Mechanism

All bodily functions are regulated through neural circuits that communicate via electrical impulses. Consequently, it is theoretically feasible to decode the electrical signals associated with various diseases. By extension, it may be possible to target and modulate malfunctioning neural pathways using microelectrodes to correct these dysfunctions. This precise manipulation of the nervous system, aimed at specific action potentials within neural circuits, could be utilized to influence a wide range of physiological processes. Examples include the regulation of appetite, blood pressure, and the stimulation of insulin release in response to elevated blood glucose levels. An effective strategy involves isolating and modulating the nerve bundles that transmit efferent signals involved in these processes [14]



Advantages

- The advantages of innovative techniques in the medical field have significantly reduced the discomfort associated with disease treatment approaches.
- The implant delivers targeted therapy by modulating neural signals directed toward specific organs.
- The device is designed to have minimal or negligible adverse effects.
- It addresses and potentially overcomes the limitations and challenges associated with traditional pharmaceutical dosage forms[15].

Disadvantages

- The high cost of bioelectronic devices is a major consideration; damage to any single component within the chip can compromise the entire system, as observed in the case of bionic eye technologies.
- The densely packed configuration of nerve and cardiac systems in these devices means that non-selective stimulation can produce unintended and potentially harmful effects.
- There is a risk of electrical shock associated with the operation of these devices.
- The implantation process carries potential risks of physiological harm to the patient.[17]

Technology of bioelectronics

Bioelectronic medicines represent a distinct category of therapeutics, integrating both electronic devices and pharmacological agents. These interventions, which may not always fall under traditional pharmaceutical classifications, leverage micro-sized devices to interface with neural pathways for diagnostic, monitoring, and therapeutic purposes. These devices can be implanted directly onto nerves or positioned transcutaneously to modulate neural activity. By precisely altering nerve function, bioelectronic medicines can influence organ systems and potentially modify or ameliorate pathological conditions with reduced incidence of adverse effects compared to conventional pharmaceuticals[18]. There are various technology used in bioelectrical medicines i.e

Advancement

Numerous devices are already available as wearable technologies that provide insights into bodily functions. For instance:

- Set Point pioneered the development of the first self-contained, rechargeable bioelectronic device designed for placement on the vagus nerve to administer electrical pulses.
- Google has recently introduced a contact lens capable of monitoring glucose levels.
- While some devices currently interface with smartphones or computers, researchers aspire to create models that operate autonomously, potentially without the need for wires or batteries.[13,14]

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