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Review Article

Recent advances in polymeric biomedical materials for the early diagnostic monitoring of acute kidney injury and COPD

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ABSTRACT
Timely treatment intervention is severely hampered by the delayed diagnosis of serious illnesses including Acute Kidney Injury (AKI) and Chronic Obstructive Pulmonary Disease (COPD). Recent developments in polymeric biomedical materials and nanocomposites designed for the early diagnostic monitoring of these complicated disorders are examined in this study. Functionalized polymers are perfect for next-generation biosensing systems because they provide previously unheard-of tunability, biocompatibility, and sensitivity. In order to identify certain physiological biomarkers, we review the literature on the integration of these smart polymeric matrices, such as responsive hydrogels, copper-functionalized carbon nanotubes, and 3D graphene-augmented polymers. These include ongoing respiratory profiles for the treatment of COPD and early-stage AKI markers such as NGAL, creatinine, and hypochlorous acid. These cutting-edge materials enable a crucial transition from reactive to predictive clinical treatment by enabling continuous, high-fidelity data collecting, which promises to improve patient outcomes and monitoring accuracy in critical contexts.

1. Introduction

Acute systemic disorders and chronic diseases are among the world's top causes of morbidity and early death, putting a tremendous burden on patients and the healthcare system. More autonomous, proactive, and reasonably priced healthcare solutions are required due to the rising incidence of these disorders, which is further exacerbated by an aging population. The clinical assessment of vital signs and certain blood biomarkers has historically been a major part of the care of both acute and chronic illnesses. However, these methods frequently fall short of providing the continuous, real-time data needed for early intervention [1]. A paradigm shift toward customized healthcare has been sparked by the combination of nanotechnologies with wearable and point-of-care bioelectronics, which has significantly improved the field of illness monitoring and management.

Since the invention of early cross-linking processes, polymers have revolutionized human life; nonetheless, their use in photonics and biosensors constitutes one of the most fascinating contemporary frontiers [2]. Because of their capacity to form porous structures, optimum optical transmittance, mechanical flexibility, and above all, sensitivity to external stimuli, polymers have become the perfect building blocks for contemporary biosensors. The physical characteristics and chemical structures of polymers can be quantitatively altered by such stimuli, which include pH, temperature, ionic strength, light irradiation, mechanical forces, and particular analytes [2]. An ideal biosensor must produce a precise, consistent, and reproducible signal in the presence of particular biological analytes. A sensor functions as a device that converts a physical measure into a signal that can be read by an observer or instrument.

In the presence of particular biomarkers, the addition of functional groups to these polymeric networks has created new opportunities for selective and reversible physical interactions. Researchers have created new methods for identifying proteins, carbohydrates, ions, and nucleic acids by incorporating functional groups into nanostructured materials such as hydrogels, nanosheets, and nanopores [2]. The utilization of functionalized polymeric materials and nanocomposites in the early diagnostic monitoring of two serious illnesses, acute kidney injury (AKI) and respiratory conditions such chronic obstructive pulmonary disease (COPD) is the main topic of this review. We look at the transition from continuous, nanoengineered body-interfaced sensing technologies to conventional, reactive clinical examinations.

2. The clinical burden of AKI and COPD and the need for advanced diagnostics

Acute kidney injury (AKI) is a serious worldwide health issue characterized by an abrupt drop in glomerular filtration rate (GFR), which significantly impairs the kidneys' capacity to eliminate toxins [3]. The risk of heart failure, myocardial infarction, and stroke is greatly increased when AKI is present. Moreover, AKI is typified by an overabundance of reactive oxygen species (ROS), which interact with proteins, lipids, and nucleic acids to cause inflammation and oxidative stress [3]. Increased serum creatinine levels and decreased urine output are key components of the clinical criteria for diagnosing AKI; however, serum creatinine shows delayed reactivity, frequently taking up to 72 hours to reflect acute renal damage. Its applicability for early clinical intervention and real-time monitoring is significantly limited by this delay [4]. When these nanoscale elements are combined with flexible, biocompatible polymeric matrices, they yield wearable and point-of-care sensors capable of unobtrusive, multimodal monitoring.

In a similar vein, respiratory conditions like COPD are becoming more problematic globally. Complex physiological issues or infections frequently impair the lung's ability to function normally as essential gas exchange chambers. Serious issues, including patient death, may arise quickly if the prognosis of these pulmonary challenges is not determined early on [5]. As a result, it is critical to continuously check respiratory functions. Researchers are making extensive use of sophisticated nanoscale sensing technologies to get around the drawbacks of conventional diagnostic techniques [2]. By using size-matched interactions with target molecules and overcoming analyte transport constraints, nanoengineered devices improve the signal-to-noise ratio to achieve higher sensitivity.

3. Polymeric nanocomposites for eespiratory and COPD monitoring

The field of wearable electronics is witnessing a paradigm change in the direction of creating novel sensor systems for the early diagnosis of respiratory conditions that pose a serious threat to life [5]. The development of point-of-care respiratory monitoring systems depends heavily on polymer nanocomposites, which mix a polymeric substance with functional nanofillers. These physical sensors are frequently used to track how environmental stimuli like strain, temperature, and humidity affect the respiratory profile [5].

For body-wearable applications, strain-based sensors are especially relevant. Polymer nanocomposite-based strain sensors are a special option for respiratory tracking because of their remarkable capacity to stretch significantly. These sensors can be applied to the patient's rib cage or directly to a facemask. The linked sensor experiences strain throughout the inhaling and exhalation processes due to the increasing expansion and contraction of the rib cage or the pressure of exhaled air inside a mask [5]. A detectable shift in electrical resistance or capacitance results from this applied strain's perturbation of the conductive filler network inside the polymer matrix. Alternative methods for respiratory profiling are provided by temperature and humidity sensors, which are commonly used as mask-based point-of-care devices. Localized temperature variations occur during intake and expiration during human breathing. A negative temperature coefficient (NTC) of resistance is frequently seen in thermally sensitive polymer nanocomposites. Exhaling causes hot air to be released, which raises the sensor's temperature and eventually lowers electrical resistance [5]. Furthermore, humidity sensors can be used to take advantage of the moisture inflow during exhale. When hydrophilic functional groups are present on the surface of a polymer sensor, moisture chemisorption or physisorption is enhanced, changing the electrical resistance of the sensor

Polymer-based respiratory sensors nevertheless confront unique difficulties in spite of these developments. During cycles of loading and unloading, viscoelastic polymers frequently show significant hysteresis. By capturing biomechanical or moisture energy from the breathing process itself, self-powered devices like Triboelectric Nanogenerators (TENGs) and Moisture Electric Generators (MEGs) provide sustainable power solutions to address powering difficulties for continuous deployment [5].

4. Advanced polymeric and nanomaterial sensors for AKI diagnostic monitoring

The early diagnostic monitoring of AKI necessitates the quick, high-sensitivity detection of particular biochemical markers in complicated biofluids like urine and serum, whereas respiratory monitoring mainly depends on physical stimuli [1]. The detection of AKI indicators such hypochlorous acid (HClO), creatinine, and neutrophil gelatinase-associated lipocalin (NGAL) has been transformed by recent advances in polymer-augmented electrochemical and fluorogenic sensors.

Since NGAL is secreted by renal tubular epithelial cells and responds to renal damage within hours, much faster than serum creatinine, it has become a prospective candidate for early AKI diagnosis [6]. Researchers have created miniature electrochemical biosensing devices using 3D microporous graphene-based electrodes functionalized with lipocalin-2 (LCN2) antibodies in order to quickly and affordably detect NGAL. Graphene's three-dimensional folding on a microporous scaffold increases the surface area per unit volume, providing an exceptionally high reactive surface area that improves sensitivity [6].

An Extreme Learning Machine (ELM) algorithm has been used to improve the performance of these graphene-based electrochemical sensors in a novel way. Researchers were able to reduce the detection limit to 0.89 ng/mL and significantly increase the area under the curve (AUC) for NGAL determination by 15% by using the ELM algorithm to remove nonzero interference factors like albumin and electrolytes from the amperometric data obtained from human urine samples [6].

For evaluating renal function, creatinine, a traditional prognostic indicator produced in muscle tissue and eliminated in urine, is still essential. Advanced non-enzymatic electrochemical biosensors have been developed by functionalizing carbon nanotubes (CNTs) with anhydrous copper acetate using a one-step hydrothermal process in order to obtain very sensitive, enzyme-free detection [4]. Numerous adsorption sites that provide particular coordination interactions between the copper nanoparticles and creatinine molecules are made possible by the special characteristics of carbon nanotubes. The sensor's high specificity and linear response in the 0.01 mM to 1.5 mM range, as well as its amazing sensitivity, are made possible by this strong electron transfer mechanism [4].

Because of its spatiotemporally limited production profile, hypochlorous acid (HClO) is an attractive early-stage AKI biomarker in addition to protein and metabolite markers. Transient HClO bursts filter straight into the urine with the onset of AKI. Researchers have created analyte-replacement fluorogenic probes, like Cy-PITC, designed for ultrafast, minute-level detection in order to catch these fleeting surges

[7]. Trace hypochlorite at ppb levels in urine can be selectively illuminated by this extremely sensitive fluorescence probe. In less than five seconds, the Cy-PITC probe, a non-invasive point-of-care diagnostic tool, can accurately differentiate between urine samples that are healthy and those that have AKI [7].

5. Polymeric prodrugs for AKI intervention and therapy

Functionalized polymers are being intensively investigated for targeted therapeutic treatments to stop the progression of AKI, in addition to diagnostics. Targeted ROS scavenging is made possible by the careful development of low-toxicity, highly renal-accumulative polymeric prodrugs [3].

TPP-HA-TK-MLT, a stepwise targeting polymeric prodrug based on hyaluronic acid, is a prime example [3]. CD44, an adhesion factor that is inappropriately overexpressed in renal tubular epithelial cells during proliferative and inflammatory renal disorders, is naturally bound by hyaluronic acid (HA). The polymeric carrier can target mitochondria and CD44 receptors sequentially by conjugating HA with triphenylphosphonium (TPP). An ROS-responsive thioketal (TK) cleavable linker connects this carrier to melatonin (MLT), a powerful ROS scavenger [3].

Upon reaching the pathological mitochondrial environment, excessive ROS trigger the cleavage of the linker, resulting in the on-demand, rapid release of melatonin to restore mitochondrial function and prevent the progression of acute kidney injury to chronic kidney disease [3].

6. Conclusions

A significant change in the treatment of both acute and chronic illnesses is being driven by the combination of functionalized polymers, conductive nanocomposites, and sophisticated machine-learning algorithms. Wearable polymer nanocomposite strain, temperature, and humidity sensors provide continuous, inconspicuous breathing pattern monitoring for respiratory disorders like COPD [5]. The creation of ultrafast fluorogenic probes for hypochlorous acid [7], copper-functionalized CNT creatinine sensors [4], and 3D graphene-enhanced NGAL sensors [6] is a significant advancement in overcoming the delayed responsiveness of conventional tests in the context of acute kidney injury. Additionally, the development of polymeric prodrugs emphasizes these cutting-edge materials' dual diagnostic and therapeutic potential [3]. As fabrication techniques become more scalable, the transition of these polymeric biomedical materials from laboratory prototypes to widely accessible clinical tools will undoubtedly transform personalized healthcare.

Authors' contributions

The author reviewed and approved the final version of the manuscript for publication.

Conflicts of interest

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