Real-time Detection of COVID-19 Aided by CNT-based Electrochemical Sensors

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University of Tehran's researchers have developed a novel electrochemical sensor modified with multi-walled carbon nanotubes. This sensor is designed for the real-time detection of COVID-19 using ROS/H2O2 species in less than 30 seconds. This product is currently introduced in the commercialization phase, after being tested on 600 cases.

The stimulation and induction of mitochondrial reactive oxygen species (ROS) overproduction in lung cells are the main side effects of the new coronavirus, namely COVID-19, which has been previously reported for SARS-CoV virus. Release of ROS from cell mitochondria leads to the activation of the NLRP3 inflammasome protein complex, as a ground for the activation of inflammatory processes in the body.

The winner of the 2019 Mostafa Award in the field of nanotechnology, Dr. Abdolahad from the Nanobioelectronics Devices Laboratory at the University of Tehran has developed and patented a novel approach (Patent pub. No: US 2018 0299401 A1, Pub. Date: Oct. 18, 2018), including an ROS/H2O2 electrochemical system, whose electrode has been modified with multi-walled carbon nanotubes. The researchers used this sensor to measure the ROS in fresh sputum samples from candidates, which is the best sample of lung epithelial cells for SARS-CoV-2. The results have been published in Biosensors and Bioelectronics journal.

This sensor was first tested for more than 140 cases, and then the sensor calibration pattern was obtained compared to the results of standard clinical tests such as CT Scan, CBC, and RT-PCR. The calibrated sensor was retested for another 30 cases with an accuracy and sensitivity of 94% and 92%, respectively, in comparison with CT Scan as the gold standard.

"In this research, we show how ROS can be used to diagnose lung diseases". Even when the symptoms of the disease are not yet known, the amount of ROS in the cases' sputum changes, and the sensor uses this indicator to diagnose COVID-19. This project is in the commercialization stage and so far, more than 600 patients have been tested in four hospitals in Iran," says Dr. Abdulahad.

Although other methods such as electron spin resonance (ESR), fluorescent-dependent methods, and chemiluminescent probes have been developed to measure ROS, none of them have the ability to measure the real-time of reactive oxygen species. The table below summarizes the advantages of this sensor over the existing methods.

Table 1- Advantages of the introduced CNT-based electrochemical sensor over other approaches

Detection Techniques	Mechanism	Advantage	Disadvantage	Application	Ref.
spectroscopic methods (Electron spin resonance or electron paramagnetic resonance)	the use of specific spin traps and probes forming paramagnetic adducts	Specific, sensitive	Expensive	Quantitative measurement of superoxide generation and oxygen consumption from leukocytes	(Roubaud et al., 1998)
fluorescent-dependent methods	oxidant sensitive probes provide enhanced fluorescence under the condition of oxidative stress generation	Quantizable of peak intensity	Low specificity	Quantifying cellular oxidative stress	(Wang and Joseph, 1999)
chemiluminescent probes	monitoring of photon generation is monitored as a result of probes reaction with reactive species	Cell permeable	Low selectivity and sensitivity	Early Diagnosis of Cancer	(Kohno et al., 2008)

spectrophotometric methods	reaction of reactive species with redox substances lead to change in absorbance	Single product, fast	Low specificity	site-specific ROS detection in lymphocytes and macrophages were obtained from the peritoneal cavity of adult male Balb/c mice	(Stockert and Blázquez-Castro, 2016)
chromatographic method	separation and identification of reactive species and product are achieved	Sensitive	Products complex	a sensitive measure of hydroxyl free radicals in Adriamycin treated rats	(Floyd et al., 1986)
electrochemical sensors	changes in oxidation/reduction current upon reactive species generation	real-time, sensitive	In some cases, complex to prepare	Real-time diagnosis of ROS in fresh sputum by electrochemical tracing; correlation between COVID-19 and viral-induced ROS in lung/respiratory epithelium	Our study

Some respiratory diseases such as asthma, acute pneumonia, and fibrosis patients with chronic Pseudomonas aeruginosa lung infection show enhanced ROS levels, while seasonal influenza, which is sometimes mistaken for COVID-19, decreases ROS levels. Therefore, regarding this difference in the mechanism of influenza infection and also the small number of conventional acute respiratory pneumonia in warm seasons, this sensor enjoys the potential to detect COVID-19 cases in less than 30 seconds.