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Review Article

Magnetic and Plasmonic properties of Inorganic Nanoparticles and their perspective in the Development of point-of-care Diagnostic approach for Covid-19

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Abstract

Due to the rise of the global controversial as a result of COVID-19 and the challenge of obtaining plausible treatment against COVID-19, the detection of virus is crucial for predicting the severity of diseases, the rate of spreading so as to overcome infections. Here in we bringing the generative inorganic nanoparticles in context of fabrication and development as point of care (POC) material for diagnostic of Corona Virus. Inorganic nanoparticles have variety unique properties such as photocatalytic, magnetic, surface plasmonic, adsorption, and surface functionalization with biomolecules ligand such as nucleic acid, protein and antibodies which enables fabrication of viral diagnostic nanomaterials. In this article we address on how the properties can be integrated in diagnostic application for detection of (SARS–COV).
Keywords: Inorganic nanoparticles; COVID-19; surface Plasmon; magnetic; point-of-care

Introduction

Point-of-care (POC) detection technologies; recently have becoming more important around the world for diagnostic of COVID-19 Indeed (POC) technology can be decentrized, rapid and sensitive, and cost effective. Inorganic nanomaterials are useful for design and development of diagnostic kits for detection of Corona Virus. In this perspective we analyze the utility of inorganic nanomaterials in diagnostic function to detect Coronavirus and as potential material for point of care detection technology. Currently available Real Time Polymerase Chain Reaction(RT-PCR) based diagnostic kits for detection of Corona virus are challenged by being time consuming (Fig 2), expensive, need an advanced equipment facilities and expertise. Fig 1 shows the cost of some diagnostic kits based on RT-PCR which ranges from 235 USD to 6,750USD.

The cost for access the Covid test and absense of enough test kit interfere checking of the diseases transmission in our communities. Therefore cost affordable and reliable techniques for detection of Corona virus infection in human is of paramount importance. In this review we address the utility of inorganic nanomaterials for Corona virus diagnostic functions. The unique properties of inorganic nanomaterials such as surface Plasmon and magnetic properties are detailed and associated with diagnostic application. Several Plasmon inorganic nanomaterials such as gold, silver and copper; magnetic nanoparticles such as iron oxide have been utilized for fabrication of point of care devices for detection of Corona virus. In this review paper the interaction of aforementioned inorganic nanomaterials with biomolecules to detect signals is one of essential area in this review. Several biomolecules such as protein, antibody, and nucleic acid are integrated with inorganic nanomaterials to provide binding area for the viral components such as spike proteins, nucleocapsid to form complex with inorganic nanomaterials. The formed complex alters the Plasmon and magnetic properties of inorganic nanomaterials hence provide signals which used for detection of corona virus. For examples Plasmon inorganic nanomaterials when integrated with colorimeter technique it provides colour changes which signify the absense or presence of virus. Magnetic separation techniques integrated with RT-PCR techniques for improvement of amplification of RNA hence to improve the sensitivity.

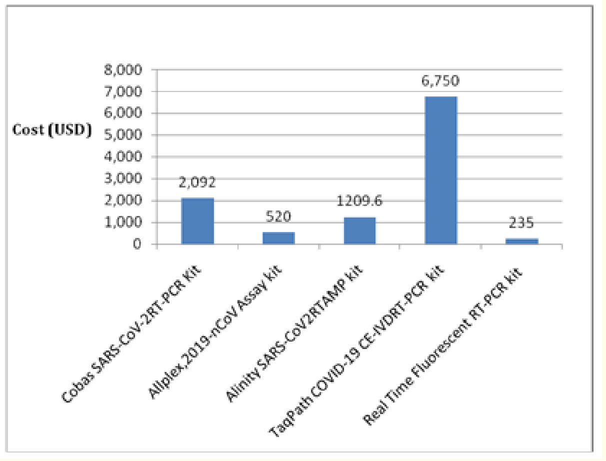

Figure 1: Real Time –Polymerase Chain Reaction based diagnostic kits cost. (https://www.theglobalfund.org/en/covid-19/health-product-supply/#products)

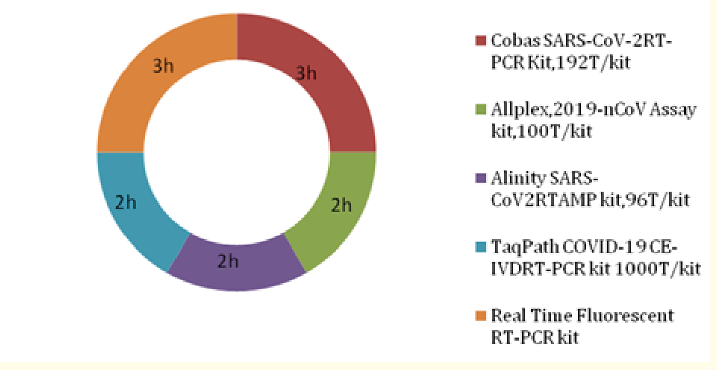

Figure 2: Real Time –Polymerase Chain Reaction based diagnostic kits assay duration.

Structure of SARS-CoV-2 and engineering of diagnostic material

SARS-CoV-2 (Fig 3) is round shaped and nano dimensional positive-stranded ribonucleic acid (RNA) viruses contain Nucleocapsid protein shell and enveloped by lipid membrane. Virus also composed with structural proteins includes glycoprotein, nucleocapsid, envelops protein, and spike protein. The outer layer of virus is constructed by spike protein.

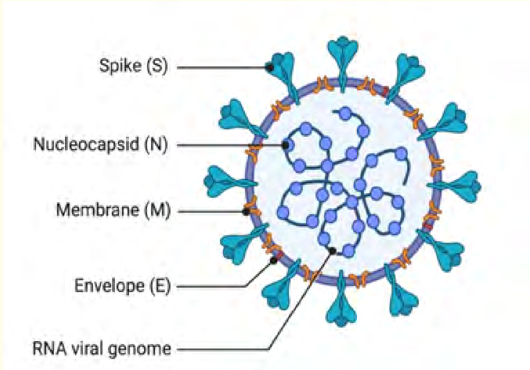

Figure 3: Structure of SARS-CoV-2.

This core-shell nano-structure and the crown-like spike protein outside of the virus surface in SARS-CoV-2 provide opportunities in engineering diagnostic material for viral detection.

Inorganic nanomaterials based diagnostic kit

Molecular technology such as Reverse Transcription Polymerase Chain Reaction (RT- PCR) testing takes a long time and has possibility to give false positive in asymptomatic recovery patients. Development of rapid accurate & reliable diagnostic tests by using inorganic nanomaterials could reduce the limitation of molecular technology based diagnostic kit. Most metal NP-based virus detection techniques were designed based on the unique optical, electrical and magnetic properties of metal NPs.

Several kinds of nanomaterials have found attractive applications *in vitro* diagnostic tests, such as metallic nanoparticles, quantum dots (QDs), silica nanospheres, magnetic nanoparticles, which belong to the zero-dimensional (0D) systems, carbon nanotubes (CNTs), silicon nanowires (SiNWs), nanopores, which belong to the one-dimensional (1D) systems, and graphene, nanostructured surfaces, and metal films, which belong to the two-dimensional (2D) systems.

Metals, especially gold and silver, have the advantageous ability to interact with external fields such as light, radiofrequency, and X-rays. Under a specific wavelength, metals exhibit surface Plasmon resonance (SPR), the oscillation of free electrons in a particle's surface; thus, they can successfully be combined with conventional methods such as colorimetric or absorption spectroscopy.

Some inorganic nanoparticles such as Super Paramagnetic Iron Oxide Nanoparticles (SPION) and silver nanoparticles have been incorporated with RT-PCR, techniques for enhancement of the detection of SARS-CoV-2. Table1 describe some commercial SARs-CoV-2 diagnostic kits which integrate inorganic nanoparticles.

Commercial Test kit	***Detector***	***Amplification nanomaterials***	***Reference***
OPTISARS –CoV-2 RT-PCR test	Detection of viral RNA	Super paramagnetic Iron Oxide Nanoparticles (SPION)	(Mascuch et al.) [15]
Ampli Max Viral RNA kit	Detection of viral RNA	Super paramagnetic Iron Oxide Nanoparticles (SPION)	(Bahadur et al.) [2]
SARS-CoV-2-Antigen	Nucleocapsid protein	Silver	(Mina et al.; Grant et al.) [17, 7]

Table 1: Some commercial SARS-CoV-2 test kit with nanomaterials for detection amplification.

Surface Plasmon based diagnostic material

Bulk noble metals such as silver, copper and gold are known for their high thermal and electrical conductivity, specific mechanical properties, and high reflectivity of incident radiation. These properties are caused by their crystalline structure and presence of delocalized electrons—existence of electron gas. With decreasing thicknesses of metal films, new properties of the material can be observed (Kvítek et al.) [12].

Surface Plasmon is defined as a charge-density oscillation at the interface between two media, with dielectric constants of opposite signs which produce a surface Plasmon wave (Pattnaik and Shrivastava) [19]. Metal –dielectric interface generate electromagnetic field of surface Plasmon wave with maximum intensity which decrease exponentially with variable penetration from 100 to 600nm (Jain et al.) [10]. Generally refraction normally detected when light strikes onto metal film. The change in localized surface Plasmon resonance depends on the refractive index of the surrounding media and the degree of the nanoparticles aggregation, which facilitate the detection of microbes. Aggregation of nobles metals induces a red shift accompanying with color changes which can be observed by naked eyes (Medhi et al.) [16].

Propagation of the SPW is sensitive to changes in the refractive index of the dielectric. The binding between the analytes and bioreceptors immobilized on the sensing surface causes a local change in refractive index (Mariani and Minunni) [14].

Several biomedical application utilizes SPR-technique including detection of microbes. Table 1 describe different Plasmon material and their application to detect several biomolecules in diagnostic application. For example surface plasmon resonance (SPR) –based biosensor was used to detect Escherichia coli O157:H7 spiked in milk, apple juice and ground beef extract using specific antibodies (Mariani and Minunni) [14].

Some diagnostic techniques such as Colourimetry-based assay can take short time within 10 minutes to detect Corona Virus. For example a colour change observed when Gold –nanoparticles functionalized with a special nucleic acid sequence of nucleocapsid phosphoprotein of the SARs-COV-2 virus. When the viral RNA is isolated from infected sample and mixed with Gold-Nucleic acid complex the colour of solution turn from purple to blue (Gupta et al.) [8] Viral RNA is isolated from the nasal or oral swab from the patient. The capped gold nano particle binds to the target protein forming agglomerate. Thus the colour of t he solution changes from purple to blue.

Generally colorimetric techniques have been applied for detection of Plasmon nanomaterials to detect colour change at a particular characteristic wavelength. When plasmon nanomaterials functionalized with signal ligands such as biomolecules they develop characteristic wave length associate with specific colour which normally changes when interact with virus.

The colour of AuNPs changes in the ultra violet and visible (UV- Visible) wavelength range and the shift in their local surface Plasmon resonance (LSPR). Since there are similarities in structure, this can also be applied to develop SARS-CoV-2 kits with some modification (Srivastava and Kumar) [21].

Plasmon material	***Detector***	***References***
Multilayered configuration consisting of TiO_2–Ag–$MoSe_2$ graphene with a BK7 prism	Immobilized CR3022 antibody molecules for detecting SARS-CoV-2 antigens (S-glycoprotein) are used for this sensor	(Moznuzzaman, Khan and Islam) [18]
Graphene sheets	SARS-CoV-2 spike antigen	(Taha et al.) [22]
Gold nanoparticles	Covid-19 RNA	(Taha et al.) [22]
Colloidal gold nanoparticle-based lateral-flow (AuNP-LF)	Detection of the IgM antibody against the SARS-CoV-2 virus	(Huang et al.) [9]
Au-NPs embedded in the nitrocellulose test strip detect COVID-19 biomarkers (IgG and IgM), which are released on interaction with antibodies embedded in the strip, eliciting a color change	(IgG and IgM),	(Singh et al.) [20]

Table 2: Plasmon material and their application to detect several biomolecules in Coronavirus diagnostic application.

Magnetic Nanoparticles based diagnostic material

It is well known that magnetic nanoparticles (MNPs) have been widely applied in microbial detection function due to ability to generate MRI contrast imaging. Furthermore magnetic nanoparticles such as iron oxide have been used for separating biomolecules such as RNA in detection of virus. Magnetic nanoparticles are integrated with Real Time-Polymerase Chain Reaction (RT-PCR) to facilitate the detection of the corona virus.

Biosensor utilizing γ-Fe_2O_3 nanoparticles as a detection medium has been reported by Maciel *et al*., [13] They used γ- Fe_2O_3 as an adsorbent of DNA. The PCR and electrophoresis assays were applied to detect the nanocomposites of the γ-Fe_2O_3 and DNA. The magnetism also endows some special characteristics to the MNPs, such as magneto-optical (MO) property (Chen, Yang and Lin) [4].

Exposing magnetic nanoparticles to the magnetic field induces their alignment with direction of magnetic field and the nanoparticles turn to anisotropic. When the light strikes on the anisotropic medium the speed of light will be governed by its polarization. If the applied magnetic field is perpendicular to the propagation of light, the phenomenon is called CM effect which can be used to detect IgG, IgM and other different. Chen et al., (Chen, Yang and Lin) [4] fabricated a magneto-optical biochip and utilized the MO CM effect to detect the spike glycoprotein of SARS-CoV-2. The biochip comprised gold nanostructure and γ-Fe_2O_3@Au core/shell nanoparticles. In fabricated biochip the gold binds with biomolecules while the maghemite core provided strong magneto-optical properties (Chen, Yang and Lin) [4].

Magnetic nanoparticles have received significant attention in the field of diagnostic. Aggregation of magnetic nanoparticles in tumor tissues can be achieved by conjugating nanoparticles with tumor targeting peptides or antibodies.

Magnetic materials provides several impressive utility for biomedical detection when applied as solid support integrated with transducer material or can be mixed with the sample and attracted by magnetic field on the surface of the detector. Biomolecules like antibodies, enzymes or oligonucleotides are immobilized on magnetic particles. Ability to form imaging contrasting and magnetic separation makes magnetic nanoparticles as potential tool for diagnostics application. For example integration of iron oxide nanoparticles with PCR-assay for detection of Corona Virus facilitated the selectivity of the target cDNA of SARS-CoV-2 in the separation process as shown BY figure 4. below (Medhi et al.) [16].

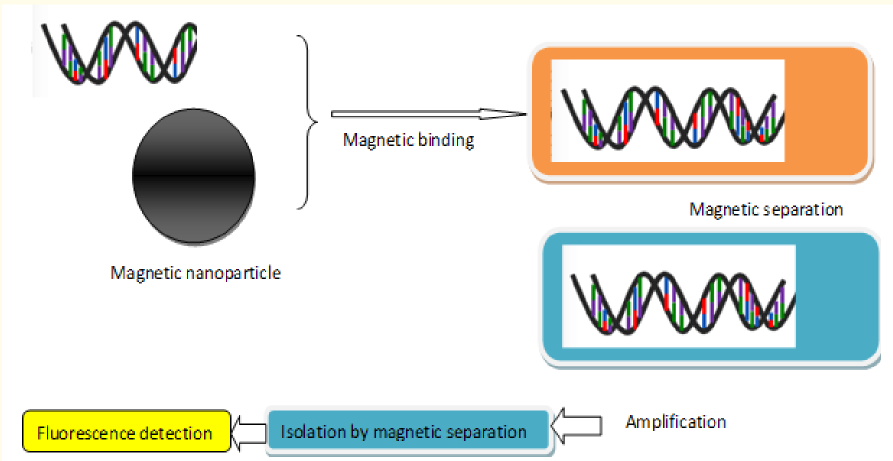

Figure 4: The Magnetic binding and separation to Origonucleotide in SARS-CoV-2 detection application Origonucleotide.

Another magnetic property which has raised interest in detection application is imaging contrasting. This property is applied in diagnostic tool referred to magnetic resonance imaging to detect the structure and composition of diseases tissues. MRI has been used as versatile tool for detection of cancer cells.

Magnetic based kit	***Detector***	***References***
Magnetic Chemiluminescence Enzyme Immunoassay	IgM and IgG antibodies against SARS-CoV-2	(Koteswara Rao) [11]
MNP-APTES	RNA extraction along with rt-pcr for SARs-CoV-2 detection	(Chacón-Torres et al.) [3]
Magneto resistive biosensor	Viral Genome ssRNA	(Tharayil et al.) [23]
Magneto-optical biochip	SARS-CoV-2, Spike protein	(Chen, Yang and Lin) [4]
Magnetic beads support immu-nological chain & secondary antibody.	Spike protein	(L. Fabiani et al.) [5, 6]
Magnetic beads combined with carbon black based screen printed electrodes	SARs-CoV-2 detection in saliva	(Laura Fabiani et al.) [5, 6]

Table 3: Magnetic material and their application to detect several biomolecules in Corona virus diagnostic application.

Conclusion

In this review we have emphasized on utility of inorganic nanoparticles in Corona virus diagnostic application. By now one of the strategy of combating COVID-19, is to monitoring the severity by using diagnostic techniques. The popular techniques which apply Real Time polymerase chain reaction has been challenged by the factors such as time consuming, expensive, need expert ties among other. In this milieu, nanotechnology can play a big role in developing diagnostic kit for detection of Corona virus. Inorganic nanomaterials reviewed in this paper could provide a promising material for development of alternative diagnostic kit for Covid –detection. Indeed the generated kits could be utilized as point care for community detection of the virus as an advance stage before go to an authorized center.

Future prospective

Since eruption of Covid-19 pandemic the popular detection method of Corona virus remains a challenge to health platforms due to some limitations include access of facilities, expense, and time of results feedback among others. In future POC Device will successful overcome the addressed challenges and strategically improve Covid-19 care, reduce costs, and remain an important pandemic monitoring because even vaccinated patients, while asymptomatic may still carry and transmit live virus.

Acknowledgements

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Volume 2 Issue 1 January 2022