Nanotechnology and Treatment of Covid-19

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ABSTRACT

Nanotechnology has indeed fulfill many roles in many fields in contemporary science, such as electronic and IT applications, medical and health care applications, including COVID-19, Energy applications, environmental remediation, nanocomposites, herbal nano-particles. Research in this field needs to further proliferate, because of the novel properties of nano-based materials. Nanotechnology, will continue to solve many technologically driven process in contemporary science. It remains the vision of contemporary nanotechnologist to proliferate this research to other dimensions such as finding a cure for COVID-19. Nanotechnology/nanoparticles is the way forward to neutralize and eradicate SARS-COV-2 virus. Nanoparticles are of the same dimension as the SARS-COV-2 virus and thus this will promote effective interaction with the virus. Research in this area is continually increasing. In addition, a relatively large number of nanomolecules can be in effective contact with the virus of nanodimensions. Of greater significance, the use of plant extracts in synthesis of plant based nanoparticles to eradicate the viruses because of their easier synthesis, environmentally friendly nature and superior nature, as selective plants possess antiviral activities on their own.

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Introduction

Nanotechnology, a relatively new area of study and research, is the “design, production, characterization, and application of structures, devices and systems, by controlling shape and size at the nonometer scale [1]. The particle matter usually range from 1 to 100 nm in size. A nanometer (nm) is a billionth of a meter, 10⁻⁹. Within this range, materials may have properties considerably different from those expected when they have larger dimensions. Nanoscience depends on the fundamental properties of nano size objects [2-3]. Nanomaterials can show atom-like behaviours, which result from higher surface energy, due to their large surface area. This is in contrast to bulk material which has constant physical properties, regardless of its size. At the nanoscale, this is not often the case [4]. Novel applications of nanoparticles and nanomaterials are expanding rapidly in many frontiers, due to their completely new or enhanced properties, depending on size, their distribution and morphology. Nanotechnology has found applications in many realms. These include health care, medicinal applications such as antibacterial, antiviral, antifungal, anti-inflammatory activities, cosmetics, biomedical, food and feed, drug-gene delivery, environment, health, mechanics, optics, chemical industries, electronics, space industries, energy, science, catalysis, light emitters, single electron transistors, non-linear optical devices and photo-electrochemical applications, environmental remediation, space technology [5-7].

Types /Classification of Nanoparticles

Nanoparticles can be broadly divided into various categories, depending on their morphology, size and chemical properties.

Based on their physical and chemical characteristics, some of the well known classes of NPs are as follows: Carbon based nanoparticles, ceramic nanoparticles, semiconductor nanoparticles, polymeric nanoparticles, lipid based nanoparticles. This paper focuses on metallic nanoparticles and plant based nanoparticles in contemporary sciences.

Metallic Nanoparticles

Metal NPs are purely made from metals precursors. Due to well-known localized surface plasmon resonance (LSPR) characteristics, these NPs possess unique optoelectrical properties. NPs of the alkali and noble metals i.e. Cu, Ag and Au have a broad absorption band in the visible zone of the electromagnetic solar spectrum. The facet, size and shape controlled synthesis of metal NPs is important in present day cutting-edge materials. Due to their advanced optical properties, metal NPs find applications in many research areas. Gold NPs coating is widely used for the sampling of SEM, to enhance the electronic stream, which helps in obtaining high quality SEM images [8].

Metallic nanoparticles have been extensively studied, because of their unique physiochemical characteristics such as catalytic activity, opto-electronic properties, antibacterial and magnetic properties [9-13]. Noble metallic NPs, such as Ag, Au, Pd have received increasing interests in the scientific community [14-15]. Their applications are seen in fields such as biomedicine, catalysis, preparation of nanocomposites with tunable electrical conductivity, thermal conductivity, tensile strength, superior rigidity, hardness and erosion resistance, manufacturing of satellite components, aircrafts spares, microchips processors [16-21]. The metallic nanoparticles are considered the most promising, as they possess remarkable antibacterial properties due to their large surface

area to volume ratio which can counteract growing microbial resistance against metal ions, antibiotics and the development of resistant strains [22]. Of these metallic nanoparticles, silver nanoparticles stand out, because of their unique properties, such as chemical stability, good conductivity, catalytic, antibacterial, anti-viral, antifungal and anti-inflammatory activities. They are usually found, as component of composite fibres, cryogenic superconducting materials, cosmetic products, food industry and in electronic components [23-24]. Ag nanoparticles have found applications in the biomedical field such as in wound dressings, topical creams, antiseptic sprays and fabrics. Ag nanoparticles display a broad biocidal effect against pathogenic microorganism via a disruption of their unicellular membrane. Hence, disturbing enzymatic activities. Ag nanoparticles have also been successful in the cancer diagnosis and treatment as well [25-26].

Synthesis of Nanoparticles

There are basically, three broad ways of synthesizing metal nanoparticles: chemical, physical and green synthesis. Chemical and physical methods are quite expensive and potentially hazardous to the environment and involve the use of toxic and perilous chemicals that are responsible for the various biological and environmental risks. Physical synthetic methods include inert gas condensation, severe plastic deformation, high energy ball milling and ultrasonic shot peeling [27]. Commonly grinding process and pyrolysis can be used. However, physical synthesis haven't been reliable to obtain metallic nanoparticles. The particles are

usually larger than 100nm which is not nanometer size. Physical methods are expensive and cumbersome for large scale production of nanoparticles [28]. In addition, "physical approaches: require enormous consumption of energy to maintain the high pressure and temperature used in the synthesis. Chemical synthesis of nanoparticles, involve the reduction of chemicals electrochemical methods and reduction of phytochemicals microemulsion, chemical coprecipitation, chemical vapour condensation, pulse electrodeposition [29-31]. A typical nano-chemical procedure, involves growing nanoparticles in a liquid medium containing various reactants, in particular reducing agents such as sodium borohydride or potassium bitartrate or methoxy polyethylene glycol or hydrazine [32-33]. To prevent the agglomeration of metallic nanoparticles, a stabilizing agent such as sodium dodecyl benzyl sulphate or polyvinyl pyrrolidone is added to the reaction mixture. Hence, chemical methods used for the synthesis of the nanoparticles are too expensive and involved the use of toxic and hazardous chemicals that are responsible for environmental and biological risks. Chemically, nanoparticle can be classified as "bottom up" and "top down" by the direction of nanoparticle formation, Scheme 1. The bottom up reaction begins from the atomic level, through forming molecules. In the top down approach, the scale of the resultant nanoparticles is larger, so that a mechanical process or the addition of acids is required to reduce the particle size. The "top down" technique requires the use of complex and complicated instrumentation [34].

Scheme 1: The synthesis of nanoparticles via the "top to bottom" and "bottom to up" approach

Green synthesis of nanoparticles

Green and biogenic bottom-up synthesis attracting many researchers due to the feasibility and less toxic nature of processes. These processes are cost-effective and environmental friendly, where synthesis of NPs is accomplished via biological systems such as using plant extracts. Bacteria, yeast, fungi, Aloe vera, tamarind and even human cells are used for the synthesis of NPs. Au NPs have been synthesis from the biomass of wheat and oat and using the microorganism and plant extracts as reducing agent [35-36]. Thus, its necessary to use safer (environmental and biological) and cost effective methods to synthesise metallic nanoparticles. This has given birth to the synthesis of nanoparticles using "Green Chemistry". The advancement of "Green Chemistry" over chemical and physical methods, for the synthesis of metallic nanoparticles is environmentally, biologically friendly. Also, its cost effective, and can be scaled up for large scale synthesis of nanoparticles. In addition, there is no need to use high temperature, pressure, energy and toxic chemicals [37]. Development of plant based nanoparticles has many advantages over conventional physico-chemical methods and has various applications in medicine and biology. For the synthesis of plant based nanoparticles, the following are necessary: (1) metal salt, (2) a reducing agent, and (3), a stabilizing or capping agent for controlling the size of nanoparticles and preventing their aggregation [38]. Plant parts such as leaves, fruits, seeds, stems, flowers, roots, barks, and fruit peels are involved in the synthesis of various types of nanoparticles [39-43]. Nanoparticles such as silver from silver nitrate, gold from gold chloride, zinc oxide from zinc nitrate and zinc acetate, cadmium sulfide and zinc sulfide from cadmium sulfate and zinc sulfate respectively are synthesized with the help of different types of plants and their different parts are reported.

Synthesis of Plant Based Nanoparticles for Combat against SARS-COV-2

Plant parts such as leaves, fruits, seeds, stems, flowers, roots, barks, and fruit peels are involved in the synthesis of various types of nanoparticles. Table 1.0, shows some selected plants used in the formation of plant based nanoparticles, PBNP. Nanoparticles such as silver from silver nitrate, gold from gold chloride, zinc oxide from zinc nitrate and zinc acetate, cadmium sulfide and zinc sulfide from cadmium sulfate and zinc sulfate, respectively, are synthesized with the help of different types of plants and their different parts are reported. Scheme 2 shows a possible mechanism of formation of Cu and ZnO NPs by using extract of plants, whereas Figure 1 shows some natural products responsible for the formation of plant based natural products. Figure 2 shows the protocol for the synthesis of plant based nanoparticles.

Scheme 2: Possible mechanism of formation of Cu and ZnO NPs by using extract of plants

Figure 1: Natural Products That Can Aid In Nanoparticles Formation

Table 1: Plant Based Nanoparticles

Plants	Plant Parts	NPS	Size (nm)	Morphology
<i>Eichhornia crassipes</i>	leaf	ZnO	32	Spherical
<i>Trifolium pratense</i>	flower	ZnO	60-70	Spherical
<i>Aloe vera</i>	leaf	ZnO	25-40	Spherical
<i>Boswellia ovalifoliolata</i>	stem bark	ZnO	20	Spherical
<i>garlic (Allinum sativum)</i>	leaves	ZnO	14	Spherical
<i>Magnolia kobus</i>	leaves	Cu	37	Spherical
<i>Potato</i>		ZnO	20	Hexagonal (wurtzite)
<i>Aloe vera</i>	flower	Cu	40	Spherical
<i>Potato</i>		Fe ₃ O ₄	40	Spherical
<i>Kalopanax pictus</i>	leaves	MnO ₂	19.2	Spherical
<i>Diopyros kaki</i>	leaves	Pt	2-20	Spherical-plates
<i>Tradescantia pallida</i>	leaves	ZnO	23-27	rod
<i>Magnolia kobus</i>	leaves	Ag	16	Spherical
<i>Kalopanax pictus</i>	leaves	Ag	10	Spherical
<i>Kalopanax septemlobus</i>	leaves	Ag	30.8	Spherical
<i>Calotropis procera</i>	leaves	Ag	10	Spherical
<i>Alternanthera dentata</i>	leaves	Ag	10-80	Spherical
<i>Cocous nucifera</i>	flower	Ag	22	Spherical
<i>Abutilon indicum</i>	leaves	Ag	7-17	Spherical
<i>Quercus brantii (oak)</i>	leaves	Ag	0.83-6	Spherical
<i>Cycas</i>	leaves	Ag	2-6	Spherical
<i>Punica granatum</i>	peel	Cu	15-20	Spherical
<i>Ananas cosmosus</i>	fruit	Ag	5-30	Spherical
<i>Vitis vinifera</i>	fruit	Se	3-18	Spherical
<i>Carica papaya</i>	leaves	ZnO	50	Spherical
<i>Banana</i>	peel	CuO	23	Spherical
<i>Belgian endive</i>	leaves	Ag	19-64	Spherical
<i>Sasa borealis</i>	leaves	Au	10-30	Oval, Spherical
<i>Elettaria cardamomum</i>	seed	Au	15.2	Spherical
<i>Camellia japonica</i>	leaves	CuO	15-25	Spherical
<i>Ficus carica</i>	fruit	Ag	54-89	Spherical

Figure 2: Protocol for the Synthesis of Plant Based Nanoparticles

Characterisation of Nanoparticles

Whatever, is the route of synthesis, nanoparticles are usually characterised via the following techniques: UV-visible spectrophotometry, Powder X-ray diffraction (XRD), dynamic light scattering (DLS), X-ray photoelectron spectroscopy (XPS) Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), transmission electron microscopy (TEM), and energy dispersive spectroscopy (EDS).

Nanotechnology & COVID-19

There is an urgent need to find a drug, combination of drugs or a vaccine to eradicate the SAR- COV-2 virus and thus present a cure for COVID-19, the planet threatening disease. Coronavirus disease 2019 (COVID-19) is an infectious disease induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [44]. It is said to be a mutant of SARS-CoV-1, the virus that causes SARS. It was first identified in December 2019 in Wuhan, Hubei, China, and since then has resulted in an ongoing pandemic [45]. As of 14 October 2020, 38.1 million cases have been reported across 188 countries and territories, but the WHO estimates that around 800 million people in total may have been infected, with the mortality being 1.08 million people with more than 26.4 million persons recovered [46]. A person can be symptomatic or asymptomatic showing symptoms of fever, cough, fatigue, shortness of breath or breathing difficulties, loss of smell and taste, acute respiratory distress syndrome (ARDS), cytokine storm, multi-organ failure, septic shock, and blood clots. The virus may incubate from one to fourteen days [47-48]. As an infectious disease it is spreads most often when people are physically close. It is said to be airborne for awhile, requiring particulate matter for transmission. It spreads very easily and sustainably through the air, primarily via small droplets and sometimes in aerosols, as an infected person breathes, coughs, sneezes, talks, or sings and enters the body via the eyes, mouth and nose49-50. It may also be transmitted via contaminated surfaces. It is diagnosed by

real-time reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab. Also, via the use of Chest CT imaging. Recommended measures to prevent infection include frequent hand washing, social distancing, quarantine, covering coughs and sneezes, and keeping unwashed hands away from the face. The use of face masks or cloth face coverings has been recommended by WHO and CDC in any public settings. Medical-grade face masks, such as N95 masks, should be used only by healthcare workers, first responders, and those who directly care for infected individuals. Whilst, these preventative measures are in placed, there are no proven vaccines or specific treatments for COVID-19 yet. It is anticipated that the first vaccine should be out before December, 2020. In pursuit of a cure, the used of plant extracts or parts to make plant based nanoparticles, may be one area to target. The SARS-COV-2 virus consists of a structure of a similar scale as plant based nanoparticles, Figure 3 Its anticipated that the proposed plant based nanoparticles can attach to SARS COV-2 viruses effectively, disrupting their structure and so kill the virus, under infrared light treatment. Plant based nanoparticles are expected to disable the viruses, even before they break into the body. They would be ten thousand times smaller than the width of a hair. Coronavirus studies also show the pathogen can likely survive on various surfaces for a few days, making it much more infectious. Since the viruses are on surfaces, they can be stopped from spreading by spraying down surfaces with nanoparticles. Metal nanoparticles produced using plant extracts are stable and can be monodispersed by controlling synthetic parameters, such as pH, temperature, incubation period, and mixing ratio. Biological nanoparticles were found to be more pharmacologically active than physicochemically synthesized nanoparticles. Among the various biological nanoparticles, those produced by medicinal plants have been found to be the most pharmacologically active, possibly due to the attachment of several pharmacologically active residues [51].

Figure 3: (a) Generalised structure of SARS-COV-2 virus (b) Detailed structure of SARS-COV-2 virus

Recent Advances in the Synthesis of Plant Based Nanoparticles to Combat COVID-19

At the moment, research, focusing on nanoparticles to kill viruses is developing. Nanoparticles (NPs) can offer alternative methods to classical disinfection protocols used in healthcare settings, thanks to their intrinsic antipathogenic properties and/or their ability to inactivate viruses, bacteria, fungi, or yeasts either photothermally or via photocatalysis-induced reactive oxygen species (ROS) generation. Plant based nanomaterials could be used to deliver drugs to the pulmonary system to inhibit interaction between angiotensin-converting enzyme 2 (ACE2) receptors and viral S protein. “nanoimmunity by design” can help us to design materials for immune modulation, either stimulating or suppressing the immune response, which would find applications in the context of vaccine development for SARS-COV-2 or in counteracting the cytokine storm, respectively. Nanotechnology has important roles in diagnostics, with potential to support the development of simple, fast, and cost-effective nanotechnology-based assays to monitor the presence of SARS-CoV-2 and related biomarkers. In summary, nanotechnology is critical in counteracting COVID-19 and will be vital when preparing for future pandemics [52]. The possible use of how polymer nanoparticles (nanosponges) could slow the spread of COVID-19 has been reported53. The cellular nanosponges consist of two types of cores: human lung epithelial

type II cell and human macrophage, made from poly (lactic-co-glycolic acid, PLGA) sonicated to form Epithelial-NS and M-NS, respectively. It must be noted that SARS-COV-2 is believed to enter the body through the nose, mouth or eyes. It attaches to the protein called ACE2 enzyme found in the epithelial cells of lungs, heart, blood vessels, kidneys, liver and gastrointestinal tract [53]. By covering the polymer-nanoparticles core with the outer membranes of lung epithelial cells, the viruses could be trap into it and preventing from entering the human epithelial cells. Thus, the polymer, neutralizing the virus. Thus, although the nanopolymer (nanosponger) have been proven to block a high percentage of the virus ability to enter human cells, their toxicity on human cells must be evaluated [54]. Nanotechnology can currently be used to identify those most at risk from COVID-19. Nanotechnology represents an excellent prospect for developing affordable and scalable detection methods. Nanoparticles are well known for their antibacterial properties and nanosensors can detect both bacteria and viruses at low concentrations. In a recent article published, it has been proposed that a point-of care diagnostic platform can utilize nanoparticles or magnetic levitation (maglev) to identify and evaluate future COVID-19 risks [55]. Researchers are developing a new nanoparticle coating which could severely limit the transmission of COVID-19 from various surfaces, whilst simultaneously reducing the use of harmful chemicals. The nanoparticle coating contains safe metal ions and polymers, with both anti-viral and antimicrobial properties. It could find applications in hospitals, other health care facilities, schools, airports and public transportation. SARS-COV-2 can survive on surface for a maximum of seventeen days. The coating doesn't utilize toxic or heavy metals and are thus safe in human [56]. A nanotech coating, designed to allow air filters to capture airborne or aerosolized droplets of the virus that causes COVID-19 has been reported [57]. The coating works by capturing liquids which encase the virus particles, while still allowing air to flow through unimpeded. This allows designed ventilation systems to remove the virus during normal operation, without limiting the system's ability to draw fresh air [57]. Nanomaterials, both synthetic and plant based, incorporated with copper and copper alloys, are currently being explored for their activity against coronavirus, SARS-COV-2. Copper was shown to be effective against polio virus in the late 1970s, and recently against another coronavirus, HuCoV-229E. It was found that the virus, which lives typically for around six days on a surface became inactive in sixty minutes on surfaces coated with copper alloys [58]. In addition, nanomaterials, derived from plants or synthesis can be employed in the production of vitally personal protective equipment (PPE) to help reduce the spread of COVID-19 to frontline medical and other workers. Nanomaterials can be incorporated in facemasks and other PPE to capture and immobilize viruses. Plant based gold nanoparticles can provide a rapid "on site" test result for COVID-19, in comparison to the reverse transcription polymerase chain reaction (RT-PCR) test currently used to indicate whether a patient has COVID-19 or not. The principle lies on the interaction of gold nano particles with antibodies. In the presence of further antibodies collected from patients, the nanoparticles cluster, changing the colour of the test swab from blue to red. The use of nanotechnology for the development of novel strategies in prevention, diagnosis and treatment of COVID-19 and other viral infections have been reported. In that paper, the use of nanotechnology for COVID-19 virus management via the development of nano-based materials such as disinfectants, personal protective equipment, diagnostic systems and nanocarrier for treatments and vaccine developments have been discussed [59]. Several COVID-19 vaccines have been manufactured and deployed across the globe. Others are

in the development stages, whereas others are being evaluated. One vaccine being evaluated is the messenger RNA (mRNA)-lipid nanoparticle vaccine [60]. Some anti-viral nanomaterials are shaped to engulf the SARS-COV-2-virus. In this regards, silica nanoparticles with 5-10 nm tall spikes that mesh neatly between a virus glycoproteins have been synthesized. The spikes are further elaborated with sialic acid sugars to enhance binding with antiviral compounds such as zanamivir [61]. (Peplow.M. Nanotechnology offers alternative ways to fight COVID-190 pandemic with antivirals. Nature Biotechnology 39. 1169-1175.

Conclusion

Nanotechnology has indeed fulfill many roles in many fields in contemporary science, such as electronic and IT applications, medical and health care applications, including COVID-19, Energy applications, environmental remediation, nanocomposites, herbal nano-particles. Research in this field needs to further proliferate, because of the novel properties of nano-based materials. Nanotechnology, will continue to solve many technologically driven process in contemporary science. It remains the vision of contemporary nanotechnologist to proliferate this research to other dimensions such as finding a cure for COVID-19. Nanotechnology/nanoparticles is the way forward to neutralize and eradicate SARS-COV-2 virus. Nanoparticles are of the same dimension as the SARS-COV-2 virus and thus this will promote effective interaction with the virus. Research in this area is continually increasing. In addition, a relatively large number of nanomolecules can be in effective contact with the virus of nanodimensions. Of greater significance, the use of plant extracts in synthesis of plant based nanoparticles to eradicate the viruses because of their easier synthesis, environmentally friendly nature and superior nature, as selective plants possess antiviral activities on their own.

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