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Plant Extracts Based Nanoparticles, Potential Nanomedicine in Fight Against COVID-19

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ABSTRACT

There is no declared vaccine or specific medication/medications to date, to fight COVID-19, even though the first vaccine is expected to be out before December, 2020. However, plant based nanoparticles, may be one of the medical route that scientists can pursue to eradicate this planet threatening virus. The SARS-COV-2 virus consists of a structure of a similar scale as plant based nanoparticles. Its anticipated that the proposed plant based nanoparticles can attach to SARS COV-2 viruses, disrupting their structure and so kill the virus. Plant based nanoparticles are expected to disable the viruses, even before they break into the body. Nanotechnology is the design, characterization, production/synthesis and application of structures, devices and systems by controlling the shape and size at the nanometer scale. Nanoparticles are usually synthesized by chemical methods that usually used toxic reactants/reagents as reducing agents that further produce toxic by-products, which in turn are hazardous to the environment. However, recently, there has been the used of plant extracts as an alternative, complementary source of reducing agents to reduce metal ions to the corresponding metal nanoparticles. Plants contain an abundance and diverse arrays of natural products such as alkaloids, flavonoids, saponins, steroids, tannins, coenzymes etc. that vary in concentration and type in different parts of the plants such as leaves, stems, roots, shoots, flowers, barks, fruits and seeds. These secondary metabolites can act as reducing and stabilizing agents for the bioreduction reaction to synthesize novel metallic nanoparticles. Plant based nanoparticles are less expensive to synthesise, ecofriendly and are thus less hazardous to the environment. This presentation on Green nanotechnology, surveys the use of plant extracts as possible green reagents for the synthesis of green nanoparticles to combat SARS-COV-2 virus.

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Introduction

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) [1]. 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 [2]. 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 [3]. 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 [4&5].

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 nose [6-7]. 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. 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 [8].

Nanotechnology, a relatively new area of study and research, is the "design, characterization, production and application of structures, devices and systems, by controlling shape and size at the nonometer scale [9].

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. Nanomaterials can show atom-like behaviours, which result from higher surface energy, due to their large surface area [10&11]. This is in constrast to bulk material which has constant physical properties, regardless of its size. At the nanoscale, this is not often the case [12].

Novel applications of nanoparticles and nanomaterials are expanding rapidly in many fronteirs, due to their completely new or enchanced 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 [13&14].

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

There are basically, three broad ways of synthesizing metal nanoparticles: chemical, physical and green synthesis. 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 (low cost), 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 [15].

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 [16].

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 2.0, shows a possible mechanism of formation of Cu and ZnO NPs by using extract of plants.

Table 1.0. Some Plants, Whose Extracts have been used for the Synthesis of NPS

Plants	Plant Parts	NPS	Size (nm)	Morphology
Eichhornia crassipes	leaf	ZnO	32	Spherical
Trifolium pratense	flower	ZnO	60-70	Spherical
Aloe vera	leaf	ZnO	25-40	Spherical
Boswellia ovalifoliolata	stem bark	ZnO	20	Spherical
garlic (Allinum sativum)	leaves	ZnO	14	Spherical
Magnolia kobus	leaves	Cu	37	Spherical
Potato		ZnO	20	Hexagonal (wurtzite)
Aloe vera	flower	Cu	40	Spherical
Potato		Fe_3O_4	40	Spherical
Kalopanax pictus	leaves	MnO_2	19.2	Spherical
Diopyros kaki	leaves	Pt	2-20	Spherical-plates
Tradescantia pallida	leaves	ZnO	23-27	rod
Magnolia kobus	leaves	Ag	16	Spherical
Kalopanax pictus	leaves	Ag	10	Spherical
Kalopanax septemlobus	leaves	Ag	30.8	Spherical
Calotropis procera	leaves	Ag	10	Spherical
Alternanthera dentata	leaves	Ag	10-80	Spherical
Cocous nucifera	flower	Ag	22	Spherical
Abutilon indicum	leaves	Ag	7-17	Spherical

Quercus brantii (oak)	leaves	Ag	0.83-6	Spherical
Cycas	leaves	Ag	2-6	Spherical
Puica granatum	peel	Cu	15-20	Spherical
Ananas cosmosus	fruit	Ag	5-30	Spherical
Vitis vinifera	fruit	Se	3-18	Spherical
Carica papaya	leaves	ZnO	50	Spherical
Banana	peel	CuO	23	Spherical
Belgian endive	leaves	Ag	19-64	Spherical
Sasa borealis	leaves	Au	10-30	Oval, Spherical

Characterisation of Plant based Anti- Covid-Nanoparticles

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

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 [17].

The possible use of how polymer nanoparticles (nanosponges) could slow the spread of COVID-19 has been reported*. 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 [18]. 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 [19].

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 [20].

Researchers are developing a new nanoparticle coating which could severly 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-COVID-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 [21].

A nanotech coating, designed to allow air filters to capture airborne or aerosolized droplets of the virus that causes COVID-19 has been reported. 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 [22].

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 [23]. 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.

Conclusion

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 gradually 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 and environmentally friendly nature and superior nature, as selective plants possess antiviral activities on their own.

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