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ANTIOXIDANTS: NANOTECHNOLOGY AND BIOTECHNOLOGY FUSION FOR MEDICINE IN OVERALL

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***Abstract*—Antioxidant is a chemical substance that is naturally found in our food. It can prevent or reduce the oxidative stress of the physiological system. Due to the regular usage of oxygen, the body continuously produces free radicals. Excessive number of free radicals could cause cellular damage in the human body that could lead to various diseases like cancer, muscular degeneration and diabetes. The presence of antioxidants helps to counterattack the effect of these free radicals. The antioxidant can be found in abundance in plants and most of the time there are problems with the delivery. The solution is by using nanotechnology that has multitude potential for advanced medical science. Nano devices and nanoparticles have significant impact as they can interact with the subcellular level of the body with a high degree of specificity. Thus, the treatment can be in maximum efficacy with little side effect.**

***Keywords*— Antioxidant, nanoparticle, medicine**

1.0 INTRODUCTION

A. What is Medical Biotechnology?

With the recent advancement in technology, humans have been able to achieve many glorious feet such as sending men up into space, creating nuclear energy, making smart gadgets such as smart phones and laptops to help with communication as well as making work easier, and so far to even be able to develop 3D-printers for medical purposes which is to generate lost limbs.

Specifically, for the medical biotechnology field, it has helped to change millions of lives in the past decades. A great example of that is the case study made in developing a cure for the Ebola virus outbreak in West Africa in 2014, which was creatively named as rVSV-ZEBOV vaccine [1]. This vaccine was genetically engineered from another virus called stomatitis virus, a virus that mainly infects domestic herd animals such as horses and cows, which causes inflammations to form around the inside mouth area of the animal [2].

B. What are antioxidants?

Antioxidants are the molecules which combat free radicals inside the body. Free radicals are responsible for much of the sicknesses that people experience, such as heart diseases, diabetes and the most serious of all, cancer. This happens when the level of free radicals in the body becomes too much [1].

Naturally, our bodies have its own antioxidant defence to keep these free radicals from exceeding to levels that can cause serious health problems for our bodies. Antioxidants are also found in various types of food products, namely fruits, vegetables as well as other plant-based food. On the plus side, preservation of food to increase its shelf life is another wonderful benefit of antioxidants [1].

On the topic of free radicals, these highly capricious molecules are naturally formed in our daily lives, for example, during any form of physical activities that we do and during the process where our bodies convert food into energy [2]. The outside environment also plays a role as to the exposure of free radicals, with the most notable examples being from cigarette smoke, polluted air and even the sun's light-ray. Why are free radicals a huge factor to the decline in human health? It is because of a process called oxidative *stress that* promotes cell damage. The older we get, the less active our body becomes at repairing damaged cells, thus increasing our risk of developing life-threatening diseases, like cancer, Alzheimer's disease and Parkinson's diseases. But being exposed to these free radical inducing environments will speed up that oxidative stress process [3]. Therefore, antioxidants play a very important role in ensuring that the level of free radicals in the body is maintained at a minimum.

1.1 History of Antioxidants

A. Antioxidants and the evolution of microbes to produce molecular oxygen

Generally, in the scientific community, the question of *'what started things out, production of oxygen through photosynthesis, or molecule mixtures that shields from oxygen-incited harm* has been the subject of debate for quite a while now. It has been theorized by scientists that the later compound might have existed and produced within microbes before oxygen existed abundantly on the surface of the Earth [4].

Back when the earth was in the process of terraforming naturally, there were already living cells that were present, but we're facing a huge problem. These living cells were quite susceptible to damage caused by the oxidizing environment of the Earth. Thus, these organisms developed a solution or more precisely, gained the capacity to deliver (or acquire) antioxidant intensifiers that help these organisms to survive the destructive effect of Earth's oxidizing environment. Earth was an anaerobic (or oxygen-free) planet, but thanks to evolution, microbes obtained the capacity to generate oxygen (O_2) in a process called and known today as photosynthesis. Which is the process that many plants use to make their own food using the energy obtained from the sunlight [4].

B. Antioxidants and its journey to being applied in man-made products

Antioxidants are mostly implemented in products that are consumed by humans. Antioxidants have been used in the process of preserving foods for quite some time now. The number one cause of food to go bad quickly is due to a process called oxidation. When chemicals in the food begin to react with the oxygen that is present in the air, a reaction occurs that changes the chemical composition of the food, kick starting the breaking down process [5].

Many antioxidants that are natural can be found mostly from plant-based origins, which belong to the phenolic and polyphenolic groups of compounds as well as carotenoids, which are pigments found in plants, algae, and photosynthetic bacteria. But even though antioxidants are from natural sources, there is still a long-discussed debate about whether or not the former is better than the lab-made preservatives [6]. Both of these terms, antioxidants and preservatives are used often in the food industry and frequently mistaken by most consumers as being the same. Preservatives is a term that brings a better appeal and is more direct, as being any sort of compound or substance that helps to keep food last longer. A common example of preservatives, sorbic acid, which can be found in bread and cheese, prevents the growth of mold because most microorganisms are unable to absorb sorbic acid as a source of energy [7].

For the term antioxidant, it does not have a straightforward meaning, but according to the Cambridge Dictionary, an "antioxidant" is defined as "a substance that slows down the rate at which something decays because of oxidation". The most common example of antioxidants used in the industry, vitamin C,

which are made into tablets for consumers to take as supplements. Then there is, tocopherols which are another major form of vitamin E, that helps to reduce the risk of contracting certain types of cancers, such as kidney and lung cancer.

Because the application and the wide variety of substances that exist for both preservatives and antioxidants, thus a table to differentiate both of the compounds have been made by the FDA.

1.2 Extraction of antioxidant

There are many methods of extraction for antioxidants, for example, separation. In order for this method to successfully work, a substance must be in liquid form so that the different densities will cause two mediums to separate. Hence, from there, it becomes easier to extract the wanted substance and dispose of the other or better yet, use it for a different application [7].

Other than that, another common extraction method used is what is known as the Soxhlet method. In this method, a sample is placed within what is known as a thimble-holder and during the process, the thimble-holder is filled with fresh condensed solvent that comes from a distillation flask. From there, at the point when the fluid arrives at flood level, the substance within the thimble-holder empties once again into the distillation flask bringing with it the extricated analytes in the mass fluid. In other words, repetition of the process mentioned is done until the extraction of the antioxidant is complete [8].

Another great example of an extraction method is by using what's called a DNA extraction. But with this method, one must be prepared with the amount of time and patience to obtain the required compound. Using this method, careful handling of the biological material used so that the samples do not contaminate each other. Labelling is an important step that needs to always be implemented when doing this method so no accidental contamination occurs because it can affect the final product.

It is also important to recognize the types of antioxidants that are being extracted (Figure 1). Therefore, it is important to recognize the compounds that make up an antioxidant. As with any chemical compound, the reason for this is because the molecular structure of a compound determines its function and purpose.

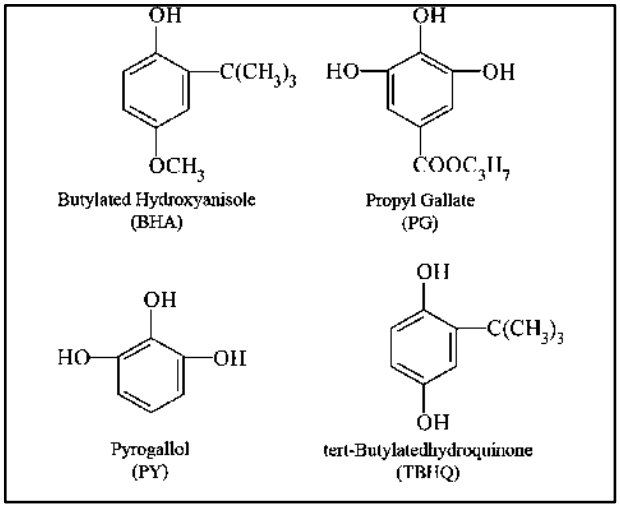

Figure 1: Shows the example of some antioxidants molecular structure [9]

There are a lot of types of antioxidants, and each one serves a different function thus, one cannot be substituted for the other when it comes to application, especially in the medical field in order to obtain a better healthy life.

2.0 INTRODUCTION

The antioxidant system is widely promoted for a good health benefit after various research provides evidence regarding the antioxidant in daily consumption. It is said to be able to prevent diseases like cancer, cardiovascular and other degenerative diseases [1]. During the twenty-first century, many studies discovered that the longevity of people improves under adequate consumption of antioxidants [1], [2]. In addition, the application of antioxidants also spreads in the food preservation process as it can prolong the life of foods [11].

As for biological processes, the antioxidant system and human body are tied towards each other as both serve a specific purpose through chemical reactions. Based on epidemiological studies, there are several of the antioxidant compounds provide a significance effect such as anti-inflammatory, antiatherosclerotic, antitumor, antimutagenic, anticarcinogenic, antibacterial and antiviral activities towards greater and lesser extent [11]. This review will briefly summarize the development of antioxidants through the fusion of biotechnology and nanotechnology which is known as nanobiotechnology.

2.1 What is Nanobiotechnology?

Recent studies have reported that nanobiotechnology has many prospects for advancing medical research and thus enhancing health care practices worldwide [12]. Biotechnology uses biological knowledge and technical skills to manipulate biochemical, genetic and genomic structures to gain sustainable competitive advantage and apply it from medicine to agriculture in a variety of fields [12]. Nanotechnology is a relatively new scientific approach, involving tools and components capable of manipulating a substance's physical and chemical properties at molecular level [12]. Thus, nanobiotechnology is nano scale biotechnology with the application of tools and methodologies of nanotechnology [13]. Furthermore, molecular or atomic evaluation machines can be made through this methodology by copying or coordinating biological processes, or by building small devices to contemplate or tweak the different qualities of the biological structure on a molecular level [11].

Biotechnology and nanotechnology are two of the most up-and-coming technologies of the 21st century which comprise nanobiotechnology and therefore able to ease other aspects in science and engineering by incorporating cutting-edge developments in information technology and nanotechnology into contemporary biological issues [11]. Currently, a multitude of therapeutic uses of nanobiotechnology, such as clinical diagnosis, target-specific drug delivery, and cell imaging, are currently being elaborately studied [11], [12].

2.2 Nano-antioxidant Delivery in Recent Therapeutic Trends

Development in nanotechnology also identified many nanoparticles from either inorganic or biological sources, such as melanin nanoparticles themselves as active antioxidants [12]. Thus, nanobiotechnology utilizes it by manipulating the molecules and atoms on substrate or nanoparticles by binding them to bio-membranes and testing where and when chemical reactions occur, in a rapid process requiring few reagents and solutions [11]. For example, if a therapeutic can be molecularly integrated to a nanoparticle, it can then be directed by radio or magnetic signals to the site of the illness or infection [11]. Extensive research on natural, synthetic and nanoparticle antioxidants and their potential in multiple applications had given new prospects and idea for the future medical technology, including gene transmission, for theranostics in neurodegenerative and cardiovascular disorders, biomedical applications, and therapy for various toxicity-induced environmental pollutants [12].

In any case, there is no examination yet, as far as anyone is concerned, on the range of nanoparticles and the method of cell reinforcement incorporation to have a total modern picture about this field in a more extensive setting [12]. Along these lines for this content, we centred around two selected techniques for the functionalization of nanoparticles with cancer prevention agents or mixes having cell reinforcement properties for the efficient and focused on conveyance with supported discharge properties [12].

2.3 Integrating Antioxidant with Nanoparticles

a) AuPN integrated Nano Antioxidant

The most scrutinized nanoparticle is gold nanoparticle (AuNP) which is inferable from its novel restorative action, latent, and nontoxic nature, hence has increased immense consideration in various fields of utilization including area of pharmacological and biomedical fields [12]. AuPNs derived from the synthesis process are also considered as effective antioxidants. Nevertheless, in order to achieve the enhanced potential in antioxidant activities, AuPNs are incorporated into natural molecular antioxidants as well as synthetic compounds of antioxidants [12]. The AuNPs were covered by polyethylene glycol (PEG) and then conjugated with the Au@PEG3SA composite antioxidant of salvianic acid A, which further boosted the radical-scavenging rate of DPPH nine times that of solely salvianolic acid A monomer [12]. In one of the enhancement of nanoparticles and antioxidant methods, the AuPNs were integrated with Trolox which derived from vitamin E as water soluble component for DPPH radical scavenging [12]. The functionalized nano antioxidant was synthesized by Au-S bonds from AuNPs and thiol ligand (Trolox) chains [12].

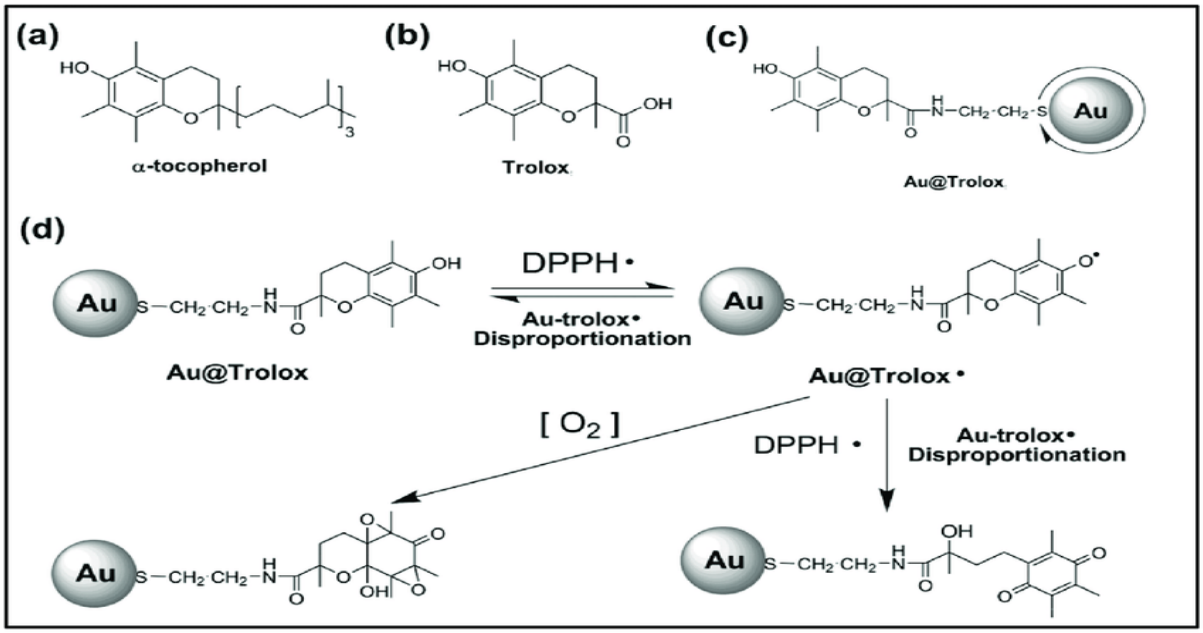

Figure 2: The mechanism of synthesized Au@Trolox and molecular structure of (a) α-tocopherol (b) Trolox, (c) Trolox functionalized AuPNs and (d) the reaction of Au@Trolox towards DPPH radical [27].

This Au@Trolox was assessed for DPPH radical rummaging tests, which exhibited higher antioxidant action by eight times higher than that of Trolox monomer, and the reason behind this effectiveness should be the organized structures of Trolox ligands on the outside of AuNPs (Figure 2) [12].

b) Cerium Oxide Nanoparticles integrated Nano Antioxidant

For this particular nanoparticle, cerium oxide (CNPs) are able to scrounge the ROS / RNS and act as antioxidant enzyme proteins, mostly based on functional physicochemical characteristics of the nanoscale substrate, oxygen absorbing and releasing ability, and the relative kinetics efficiency of redox between Ce3 + and Ce4 + ions on the CNP surface [12], [13]. CNPs have also been used extensively to treat various cancers in vitro and in vivo, including neuroblastoma, the most recently reported one [11],[12], [13]. However, the anti-cancer characteristics of CNPs rely on ROS induction and accumulation, despite corresponding decrease in antioxidative enzyme rates [12]. Thus, the combination of CNPs and curcumin in one composition with provided knowledge of curcumin which acquires anti-cancer properties can lead to enhanced physiological activity [12].

The anticancer properties of curcumin charged in nanoceria (CNP-Cur) and dextran-nanoceria (Dex-CNP-Cur) were examined in an experiment by Kalashnikova et al. In the neuroblastoma model MYCN amplified and non-amplified cell lines including the suggested form of nanoceria with its compound structural (Figure 3) [12].

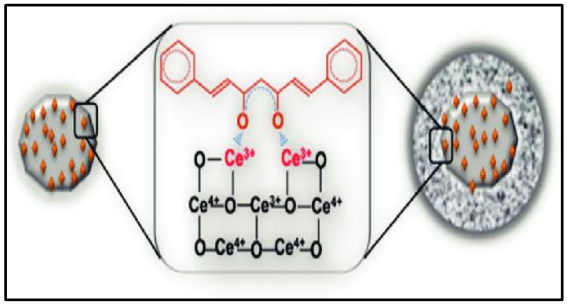

Figure 3: Suggested form of CNP-Cur (nanoceria) and its compound structural [15].

The result reported that dex-CNP-Cur has been able to induce substantial cell death in MYCN-amplified IMR-32 cells, i.e. a 2-fold and 1.6-fold reduction in viable cells for MYCN-upregulated and common cell lines, with zero or only minimal toxicity in healthy cells aside from untreated cells [12]. At these results, the significant synergistic reaction from adsorption of curcumin on the surface of ceria particles in comparison to either curcumin or ceria dependent solely [4]. This formulation proves

that this process could be further improved [14].

The development of antioxidants and its application is widely used to prevent the generation of free radicals especially in medical studies. The advancement of medical treatment is now using nano antioxidants as alternatives towards finding solutions for degenerative disease. However, further testing and experiments need to be conducted to provide a more solid foundation for the innovation in nano antioxidants for wider applications.

Nanobiotechnology is still recent in its development. The various incorporating areas of nanobiotechnology are taking nearer and closer to fruition of the science in nanoscale units [11]. Nanobiotechnology offers a vast array of medical uses especially innovations in drug delivery systems are really the first step of starting something new.

3.0 ADVANTAGES OF NANOTECHNOLOGY AND BIOTECHNOLOGY FUSION FOR MEDICINE OVERALL

3.1 The Practicality of Nano-Technology and Biotechnology Combination in Modern Medicine

The early contributors to this field of science were James Clark Maxwell, a Scottish physicist and mathematician, and Zsigmondy, an Austrian-German chemist. Zsigmondy did intense research on colloids, which are chemical substances where one substance dispersed evenly throughout another one, and also researched about gold sols as well as other nanomaterials [17].

With the catalyst set off by the scientists of the past, many modern scientists and researchers aim to improve, and to continue to improve on nanotechnology so that it can be carried into many fields of work. For example, in the medical field, nanotechnology, or more specifically nanobots have been tested upon lab rats that have cancerous tumors by carrying the medicine with great precision to the affected area within the body of the mice. This experiment was done by researchers at the Arizona State University and National Center for Nanoscience and Technology of the Chinese Academy of Science and according to them, the nanobots were made from folded sheets of DNA [18].

According to one of the researchers responsible for developing these nanobots, Guangjun Nie, the researcher says that these nanobots are able to sense their environment, navigate as if they have a GPS of the human body and carry out mechanical tasks just like their larger robot counterparts [20].

Due to some diseases that require precise measures of treatment, such as tumors and cancers, nanotechnology can help to mitigate the possibility of accidental overdose of medicine which does regularly happen when patients are not under the supervision of their doctors. Other than that, the advantages of using nanotechnology in the medical field can help to clear blockages within a patient's arteries and surgeries can be performed much faster and with keen accuracy combined with biotechnology techniques in biomolecular level. Some researchers even suggest that it may be possible to repair damaged genes, which are the primary cause of genetic conditions such as color-blindness. The possibilities of nanotechnology and biotechnology fusion with their notable advantages which it brings into the medical world is of great significance and can help to change many lives for the better [21].

3.2 Nanobiotechnology in Anti-Aging Antioxidants Delivery.

It is to say that nanotechnology can be adapted easily into the transmission or way of inserting the antioxidant into the body. Unlike the conventional method of consuming antioxidant supplements via pills, which does not necessarily distribute the medicine towards the specified place, rather distributes to the entirety of the system. To be more specific, the intake of medicine by consumption has two types of medication, which are tablets and capsules medicine. The differences between the two are shown in Table 1.

What this highlights is that the conventional methods that we have today and still use today, which is we consume medicine, either in tablet form or capsule form and rely on the substance contained within those said medicine to cure illnesses. But, with the help nanotechnology, all that could change and it could help with the distribution of antioxidant medicine, specifically for aging, to target dead cells and to rejuvenate those said dead cells, because one of the leading causes of aging and age related diseases is the amount of free radicals in the body which can cause cell to die off due to a process called oxidative stress [25].

Table 1: Differences between tablet and capsule medicine [25]

Capsules	Tablets
Consist of powder of jelly encased in a dissolvable plastic-like container.	Powdered medicine compressed into a solid form.
Cannot be divided/cut in half because contents will spill.	Can be halved/cut in two.
Enters the blood-stream immediately after consumption because it is not coated with sugar or other similar substances.	Will not immediately enter the bloodstream due to the sugar/other similar substance coating it.
Available in fewer shapes and sizes.	Available in varying sizes and shapes.
More expensive than tablet medicine.	Less expensive than capsule medicine.

Why nanotech is better than the conventional method of drug delivery? The answer is because it can reduce the risk of damaging healthy cells within the body and it could help to detect diseases earlier. There are nano-delivery systems with functionalized natural antioxidants designed for this purpose of delivering medicine to the desired cell, namely life-threatening cells like cancer, are programmed to be attracted to these diseased cells such as nanoceria. Researchers at North Carolina University are on their way to develop a method in order to deliver cardiac stem cells to repair damaged heart tissue. The researchers attach what is known as nanovesicles, which are attracted to injured tissue to increase the amount of stem cells delivered in order to fix said damaged tissue. (Nanotechnology in Medicine - Nanoparticles in Medicine, 2020).

Henceforth, it is no surprise how this technology can be applied to the delivery of anti-aging antioxidants to damaged cells because of the efficiency as well as the precision of this technique. Although it is still in development, it might soon be able to be applied in many hospitals around the world as soon as the results for this technology have more upsides than downsides.

3.3 Benefits of nano antioxidants in anti-aging medicine

In recent times, a lot of biomolecules have potent antioxidant qualities used in anti-aging research. In the scientific world, aging is a term that is defined as the systematic decline in both physiological and biochemical functions affecting all living organisms. The scientific world has been intrigued by the idea of extending the average lifespan of humans ever since the discovery of the first and one and only biologically 'immortal' jellyfish. These jellyfish are said to be able to revert back to their early stages of life again as a Polyp, which is essentially the baby stage in the jellyfish's life [19].

During the last few decades, PBPs have been extensively experimented upon to investigate their antioxidant or free radical scavenging abilities in both *in vitro* and *in vivo* experiments. It is hypothesized that PBPs antioxidant properties would differ with different mechanisms related with various constituting amino acid side chains. Meaning that the variation in amino acid distribution located on the outside surface of PBPs could lean more towards one mechanism than the other, creating diverse antioxidant activities.

This is good because scientists can then control the number of antioxidants that go into making or to be implemented into medicine or supplements for it to be effective at reducing free radicals in the body as well as being on a safe level for human consumption. Establishing the antioxidant nature of PBPs will be of great significance for therapeutics of ROS-related disorders (ROS stands for *Reactive Oxygen Species*) which have been known to be the cause of various chronic and degenerative illness such as cancer, neurodegenerative and digestive diseases [4].

4.0 EFFECT OF NANO ANTIOXIDANTS TOWARDS SOCIETY

4.1 Introduction

In the natural state of living things, aging is unavoidable as part of a natural phenomenon that occurs to all multicellular organisms with few special cases and some unicellular organisms such as bacteria, yeast and protozoa [11]. Based on recent studies, the mechanisms of aging have been identified as the accumulation of malignant transformation in cells which cause a rise towards the risk of illness and death [11]. The damaging effect of the cell is due to the reactions of free radicals and other reactive oxygen reactions. This also known as oxidative stress which many researchers had studied through various health disorders thus led to the inventions of antioxidants.

All can be seen in a simple experiment of an apple which is cut into half and turns to brown after a certain period of time. This indicates that the oxidation occurs to alter the biochemical compounds in cells as secondary products. Due to the oxygen introduced in the apple cells, it causes the polyphenol oxidase (PPO) enzymes in chloroplasts to oxidize the phenolic compounds present in apple naturally to o-quinones. Thus, the by-products from this biochemical reaction are in the form of free radicals that attack and cause damage to the cells. Same goes for the human body where aging is the form of how the process undergoes as natural phenomenon or can be related to modern health disorders.

Oxidative stress has long been associated with various illnesses and attempted to be regulated using different medicines. Conventional antioxidant therapeutics have been around for a long period of time, but alas for several possible explanations were less successful, including their failure to penetrate the blood-brain barrier, which in turn has proven them counterproductive in many neurodegenerative diseases [12].

Many studies had raised the questions regarding the antioxidant supplementation of vitamins and essential nutrients, also the effect of synthetic compounds which could lengthen the longevity of a model animal [11]. Recently, engineered nanostructured particles were found as a ground-breaking technique to amplify the functionality of novel antioxidants. Nanoparticles served as a carrier or antioxidant delivery system which have been found to be effective in promoting antioxidant activity while specific transmission of certain antioxidants showing ineffective permeation across cellular membranes and assimilation of cells. In addition, nanoparticles integrated with natural antioxidants help promote the physicochemical properties of antioxidants under synthesis conditions, perform the tasks in a broader range of intensities through intact molecular form and, most importantly, provide steady production [12].

Numerous nanosized delivery systems designed for oral phytotherapeutic administration have now entered the clinical trial stage and are now progressively being used in clinical practice [11]. Progress in nanoparticles' functional properties can be used to analyse interactions with antioxidants. Due to the small scale, high surface-to-volume ratio and electrical structure, nanoparticles have special optical, catalytic, electrical and mechanical properties [12]. The attributes and behaviours of these nanoscale materials are regulated by a different set of rules than their counterparts of a micrometer dimension, providing possibilities for innovative new developments and functional application.

Nanoparticles provide many benefits over conventional forms of distribution of antioxidants, including ecological sustainability from bioactive materials, improved bioavailability and selective antioxidant production, as well as regulated release at the delivery point [nano anti trends]. Below is the list of available nano delivery systems for nano antioxidants [12].

a) Nanoparticles functionalized antioxidant
b) Nano gel entrapped antioxidant
c) Hollow tagged nano antioxidant
d) Nanoparticles mediated antioxidant encapsulation and delivery

4.2 Application of Nanobiotechnology in Therapeutic

Biopharmaceuticals sector provides vast opportunities to develop drugs for health complications on which conventional pharmaceuticals cannot point. Thus, the application of nanobiotechnology plays a part in contributing the current tools and techniques with the knowledge of biochemistry and cell engineering. Conventionally, the pharmaceuticals industry produces and develops drugs to treat a multitude of diseases with confirmed targets. Yet only 70 to 80 percentiles of the potential of new drug formulation suffers, and these shortcomings are frequently found late in the manufacturing process, with vast amounts of money being wasted in capital expenditure [11].

Nanoscale drug development techniques will be a game changer for new businesses, which could not employ a large number of chemists or experts to synthesize thousands of compounds and analyse the potential of the new drug design[14], [15]. This nanoscale drug formulation ensures stability for defenceless compounds to denaturation when subjected to intense pH and extend the half-life of a drug by

increasing the formulation retention through bioadhesion. Based on the current modern diseases with relatively recent reports in mutation occurs provided by the surroundings factors needed the new drugs as some of the current therapies are no longer relevant. Due to this factor, it became a major motivation for all medical researchers in conducting various experiments to provide solutions with solid evidence.

4.3 Perspective on Nanoantioxidant Implementation

The natural state of antioxidants without extraction could only progress not as pure antioxidants for consumption while they are bound with few other compounds. In the antioxidant system which consist of antioxidant enzymes, nutrient-derived antioxidants, metal binding proteins and numerous other antioxidants are by far an efficient antioxidant despite readily reacting with oxygen [15]. [16], [17]. Thus, the cause of an antioxidant's key reaction surely is not about the transferring of oxygen, but instead the cause of obstruction by the autoxidation radical chain process in the fatty acid.

Nano Antioxidant is an innovative approach that enhances its capabilities to deliver antioxidant agents that pass through the membrane cell with the assistance of nanoparticles. There are some nano antioxidants being practically used in medical treatment with success outcomes such as nanoceria where cerium oxide nanoparticles conjugate with curcumin compounds. Cerium can be found in abundance of earth sources which is a rare mineral's element of lanthanide series [14], [18]. As for curcumin, it is a yellow pigmented compound which is derived from yellow coloured plants such as turmeric.

The chemical reactions of antioxidants proceed after absorption intending to provide protection for multiple compounds against oxidation. Studies showed that the majority of natural antioxidants had excess electron density within themselves which is to avert other molecules turning into radicals for extended periods of time [14], [19], [20]. Figure 4 depicts the mechanism of nanoceria acting as nano antioxidants to neutralize the oxidative stress in healthy cells [21]. The first line explained the absence of nanoceria or antioxidants; free radicals could cause damage to cells and eventually led to cell death [17], [22]. In contrast to the second line which explained the scavenging of free radicals with nanoceria which restore the cell morbidity.

Nano antioxidants possess great potential in providing a breakthrough for multitude of diseases with accurate cell targets. Biopharmaceuticals could apply nanobiotechnology as a guide for nanoscale biomedicine which is a new game changer in medical treatment. The evidence can be seen in the application of nanoceria in cancer treatment [23], [24], [25]. Among all the current methods and treatment, all efforts have concentrated on green synthesis methods to produce nanoceria using biocompatible stabilizers and generating less adverse effects. Nanoceria exhibits a notable antimicrobial activity against different bacterial species [14]. Recent breakthroughs in nanomedicine in a number of medical fields further set up the possibilities commercially available. It is currently under review for its potential use as diagnostic and regenerative [26], [27].

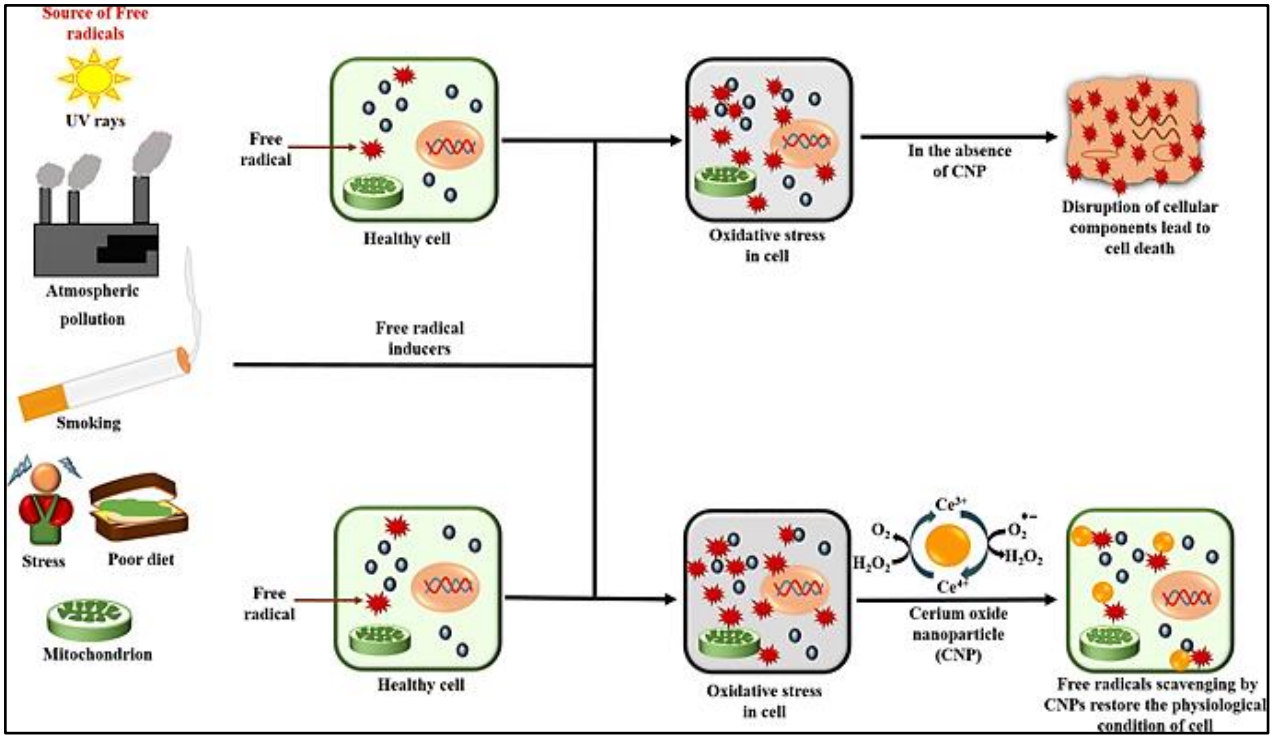

Figure 4: Mechanism of nanoceria, a) effect of ROS in healthy cells without nanoceria, and b) effect of ROS on healthy cells with the presence of nanoceria [17].

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