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Review Article

The New Era of Selenium Nanoparticles in Medicine

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Abstract

Dietary sources provide animals and humans with selenium (Se), a necessary trace element. Animals that are deficient in Se are more vulnerable to oxidative stress-related harm. A significant portion of Se is integrated into selenoproteins. Glutathione peroxidase (GPX) is the selenoprotein that is most widely known. These selenoenzymes help to eliminate hyperglycemia and hyperlipidemia, guard against the accumulation of reactive oxygen species, remove the end product of chronic oxidative stress, and prevent various cancerous changes, chronic inflammatory conditions, and cardiovascular/ atherosclerotic disease.

Nanoparticles help to improve targeting, decrease toxicity, increase bioavailability and bioactivity, and offer a variety of ways to control the release of the encapsulated component. In comparison to Se, Se nanoparticles (SeNPs) have a higher absorption level when supplemented regularly. Therefore, it is crucial to create new methods to improve the Se compounds' (selenoproteins, selenioenzymes) transit. Special consideration is given to SeNPs about their use as medicinal agents and food additives. Because of their antibacterial, antidiabetic, antioxidant, and anticancer properties, SeNPs are used in biomedicine and pharmaceuticals. Another application for SeNPs is to counteract the harmful effects of chemicals and heavy metals.

Keywords: selenoproteins, selenoenzymes, glutathione peroxidase, oxidative stress, and reactive oxygen species.

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1-Selenium (Se) as a necessary trace mineral

Cereals, grains, and vegetables are among the food sources of Se, a trace element that is vital to both humans and animals. Plants differ significantly in their Se content based on the amount of Se present in the soil. Se is mostly converted by plants into Se-methionine (Se-Met), which they then substitute for methionine (Met) in proteins. Regardless of the Se content in the soil, plant protein does not considerably incorporate Se (Se-Cystine, methyl-Se-Cystine, and γ-glutamyl-Se-methyl-Cystine). (Se) cannot be synthesized by higher mammals. [1]

The elements of Se are very significant in the domains of biology, chemistry, and physics. Se is found in nature in two forms: organic (selenometh-ionine and selenocysteine) and inorganic (selenite and selenate). In nature, Se can be found in both crystalline and amorphous polymorphism forms. The two crystalline forms of Se are monoclinic and trigonal. Red in hue, monoclinic Se (m-Se) has Se8 rings in it. It can exist in three different allotropic forms (α, β, and γ) depending on different packings. [2] At room temperature, trigonal Se, or t-Se, is the most stable crystalline form and has a black color. The non-crystalline forms of Se are vitreous, black, and red amorphous (a-Se). Figure 1(a) and Figure 1(b) show the crystal structures of t-Se and m-Se, respectively. [3]

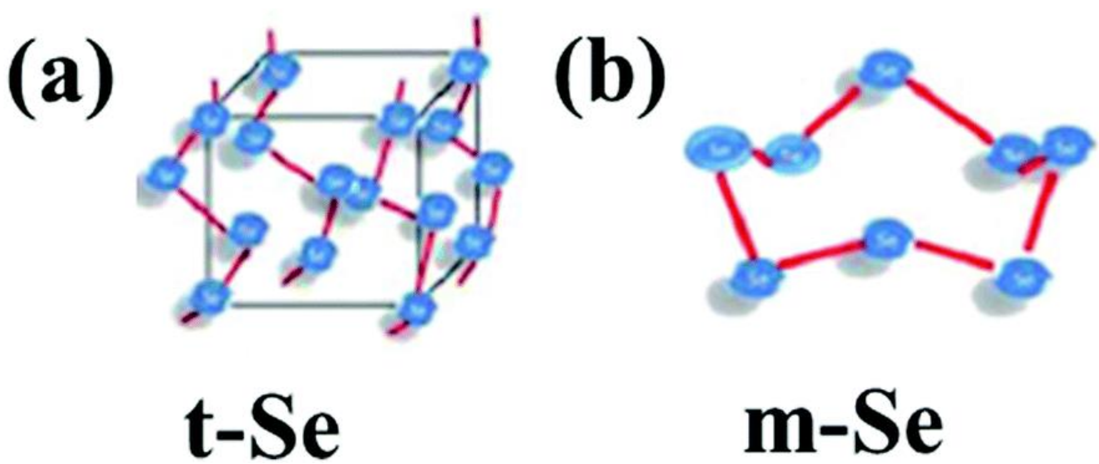

Figure 1 General representation of the crystal structure of (a) t-Se and (b) m-Se.,[3]

2- Se as a component of substances and selenoproteins

In the human body, Se is a component of Se-containing proteins and chemicals that are essential for metabolism, thyroid hormone production, DNA synthesis, reproduction, and defense against oxidetive stress and infection. It has a wide range of commercial and industrial uses.[5] Its low melting point and high photoconductivity make it highly active in organic hydration and oxidation reactions. Although Se is a necessary trace element for human health, there is very little difference between its beneficial and harmful effects. [3]

Many enzymes require Se as a necessary component, some of which have antioxidant properties. Animals lacking in the element are more vulnerable to harm from specific forms of oxidative stress. A significant component of selenoproteins is integrated by (Se), an important mineral for antioxidant defense.[4] GPX, the most well-known selenoprotein, guards against cell damage brought on by free radicals such as reactive oxygen species (ROS). The sensitive regulator nuclear transcription factor NF-kB (nuclear factor kappa-light-chain enhancer of activated B cells) is blocked from activating by Se. [5]

Additionally noteworthy about the trace element is its involvement in immune competence, namely in cell-mediated immunity, cognitive function, and cardiovascular disease prevention.[6]

When serine is deficient, the liver produces more (GSH) and releases it, which boosts plasma GSH levels and affects GSH metabolism. Elevated plasma GSH can cause cysteine depletion and limit protein synthesis.[7]

Additionally, hepatic glutath-ione-S-transferase (GST) activity rises and (GPX) activity falls with Se deficiency.[8]

The standard term for an enzyme family having peroxidase activity is glutathione peroxidase (GPX), and it serves the primary biological function of shielding the body from oxidative damage. Glutathione peroxidase is a biological enzyme that lowers free hydrogen peroxide in water and lipid hydroperoxides in their corresponding alcohols. [9]

Scientific research indicates that antioxidant enzymes such as (GPX), superoxide dismutase (SOD), and catalase (CAT) can also become less active in response to hyperglycemia. Increased levels of free radicals and proinflammatory cytokines, such as NF-κB may result from this. NF-κB stimulates apoptosis, which is carried out by cysteine proteinases (caspases), including caspase-3. [10]

The glutathione peroxidase enzyme, Se, functions as a potent antioxidant that is utilized to treat diabetic macular degeneration (DM) and its aftereffects. [11]

The word glutathione peroxidase refers to a group of related enzymes that function as antioxidants and have Se at their active site. [11]

Chronic oxidative stress ultimately results in damage to cellular lipids, proteins, and DNA. This damage can cause a variety of malignant alterations, chronic inflammatory diseases, and atherosclerotic/cardiovascular disease. These selenoenzymes aid in the treatment of hyperglycemia and hyperlipidemia by catalyzing the conversion of hydrogen peroxide to water. [12]

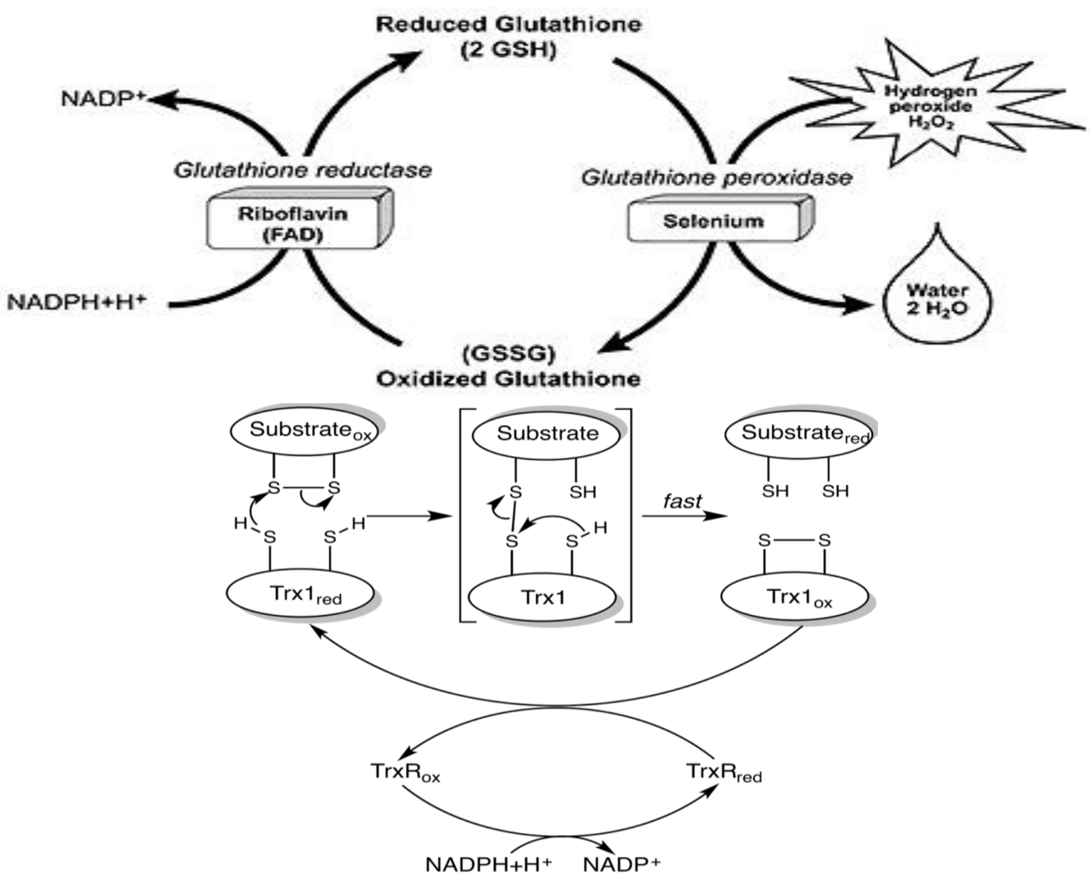

Figure 2: Glutathione peroxidase acts as antioxidants [13].

3- Development of SeNPs

Se NPs research has drawn increased attention in recent years because of its significance in numerous physiological systems. (14)

The functions of nanoparticles include lowering toxicity, increasing bioactivity, enhancing targeting, and offering a variety of ways to control the release of the encapsulated component. (15)

Because of their distinct bioactivity in nanoforms, inorganic nanoparticles of metals such as Ag, Cu, Au, Fe, Se, Ti, and Zn have a prominent position. As a result, to use nanoparticles in the environment and for medical purposes, synthesis is required. The synthesis of SeNPs is achieved using physical, chemical, and biological techniques. (14)

According to the Se absorption profile, nano-Se can cause a blue shift in the absorption spectrum, with different preparations experiencing different degrees of this shift. (16)

From this, it may be inferred that on the nanoscale, the bandgap of Se rises from 1.7 eV in bulk to 3.3 eV. (17)

Since elemental Se is the least poisonous form, its nano-form has garnered a lot of interest. It's interesting to note that functionalized SeNPs are less cytotoxic than Se inorganic Se, Se salt, Se selenite, and selenoproteins.(18)

In clinical investigations, elemental nano-sized Se may be a preferable substitute for traditional Se supplies.(19)

Fig3 shows how the cytotoxicity decreases with increasing SeNPs size. SeNPs are extremely chemo-preventive, anti-hydroxyl radicals, and physiologically active. (18)

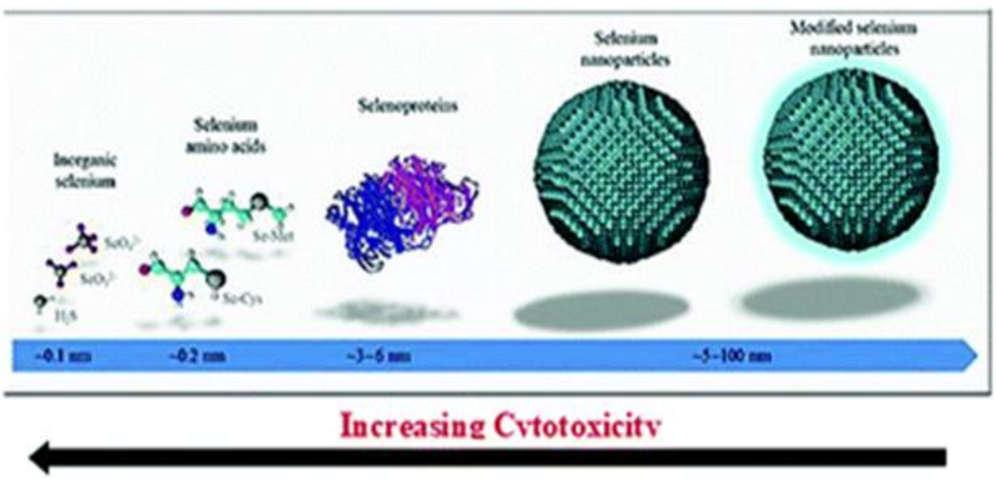

Figure 3: Extent of cytotoxicity from various sources of Se concerning their size (20).

4-Characterization of SeNPs

The techniques used to evaluate SeNPs include electron dispersive X-ray spectroscopy (EDAX), UV-vis spectroscopy, Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), X-ray diffraction (XRD), and transmission electron microscopy (TEM). These techniques have been used to investigate the many chemical and physical properties of the synthesized nanoparticles. To describe the shape of the nanoparticle, TEM and SEM are utilized. (21)

In comparison to Se, SeNPs typically have a higher rate of absorption when supplemented regularly. Thus, it is crucial to create novel methods for boosting the bioavailability, bioactivity, and regulated release of Se compounds (selenoproteins, selenioenzymes, etc.) to improve their transportation. (22) Special consideration is given to SeNPs about their use as medicinal agents and food additives. Because of its anticancer, antidiabetic, antibacterial, and antioxidant properties, SeNPs are used in biomedicine and pharmaceuticals. Additionally, heavy metals and chemicals can have harmful effects that can be countered by using SeNPs. (23)

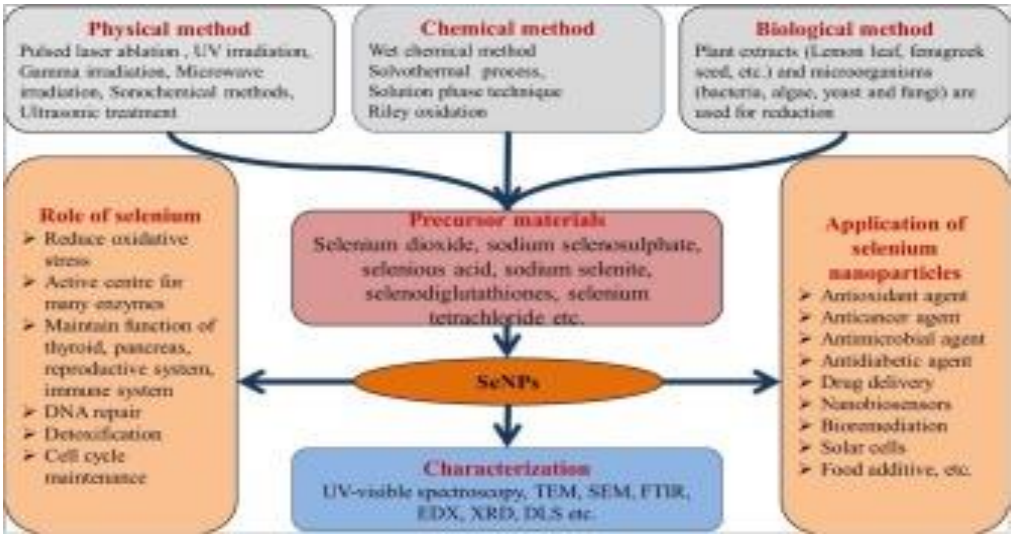

Figure 4 SE-NPs [23].

5- Biomedical applications:

SeNPs' significance at the cellular and tissue levels has drawn the attention of several researchers worldwide to their biological uses. It is commonly known that a variety of abiotic stresses can cause an excessive amount of hazardous (ROS), which can lead to damage to vital components including proteins, lipids, and carbohydrates, and cause several disorders. [23]

The global healthcare system is in jeopardy due to the ongoing growth in diseases including diabetes, cancer, and bacterial infections. To lower the worldwide death rate from cancer, different types of medicines are currently required, including chemotherapy, radiation therapy, or a combination of both .[23]

In general, there is considerable worry about the side effects of such therapy. It has been shown that taking Se supplements in addition to routine anticancer therapies increased the effectiveness of chemotherapy drugs, improving patient outcomes and overall health [21].

The effectiveness and safety of Se have been evaluated in the new clinical preliminary studies, taking into account the toxicity and viability of standard anticancer therapies [21]. Numerous super nutritional in vivo and in vitro investigations have demonstrated the anticancer effect of Se. According to reports, using selenite salt supplements can reduce the risk of liver cancer by 35%. A few studies found that the risk of prostate, lung, and colorectal cancers has decreased after taking 200 µg of Se per day in the form of Se yeasts. [20]

In a similar vein, Se supplements lower the incidence of stomach cancer. Reduced selenoprotein (SelP) dosages have been linked to an increased risk of prostate, throat, kidney, colon, and lung cancers. Brassica and allium vegetables, which are high in Se, reduce the risk of colon cancerous growth [19].

These organic and inorganic sources of Se have inferior biocompatibility and higher toxicity despite their benefits. SeNPs gained attention as a solution to these problems.[20]

As seen in Fig 5, nano-Se in the form of nanomedicine has an exceptional quality of antibacterial, anticancer, antidiabetic, antiparasitic, and antioxidant. Free radicals and (ROS) are lessened by the antioxidative qualities of nano Se. Compared to conventional therapeutic drugs, SeNPs' increased effectiveness shows enhanced medicinal benefits as cytotoxic, antidiabetic, antibacterial, and chemoprotective agents [24].

Additionally, they can be employed as theranostic and therapeutic agents. Notably, several studies on SeNPs demonstrated the properties of biomaterials interacting with tissues and cells, including decreased toxicity. SeNPs participate in a variety of oxidoreductive cycles and are naturally occurring, physiologically active substances. They also exhibit a host of regulatory effects that support the proper operation of living things, including plants, as well as a host of health benefits [25].

Studies have demonstrated the potential of (SeNPs) as an antibacterial, an anticancer therapy, and a means of preventing cancer by limiting the harm that free radicals cause to cells. These can also be utilized as components in the creation of nanobio-sensors [26].

Two methods can be used to characterize the action mechanism of SeNPs: (a) breaking down the integrity of the cell membrane by producing reactive oxygen species (ROS); and (b) changing the DNA sequence of microorganisms by inflicting damage to the cell wall and attaching to the cell membrane to prevent the growth of microorganisms [20]. Bioremediation and wastewater treatment can benefit from the cycles connected to SeNP synthesis. By working together to lessen the harmful effects of heavy metals, they can be very helpful in their treatment. The next section goes into great detail on the several applications of SeNPs based on the advantages outlined above [27].

<u>5-1- Antioxidant activity</u>

(ROS) and reactive nitrogen species (RNS) are free radicals that are often produced by several physic-cochemical and metabolic processes in the human body. The creation of deadly diseases is caused by the increased production of intermediate complexes like hydrogen peroxide and superoxide during these processes, which in turn cause damage to cells. Antioxidant substances are therefore used to stifle the production of these free radicals as well as their scavenging. [28]

On diverse human body cells, the surface of Se nanoparticles coated with different chemical compounds and plant extracts functions as both a pro- and antioxidant display mechanism. According to reports, SeNPs can play a significant role in reducing the quantity of free radicals needed to stop DNA oxidative damage in both in vitro and in vivo experimental settings. [26]

Selenoprotein has also been shown to be an important source of Se and to be involved in the synthesis of essential antioxidants such as glutathione peroxidase, thioredoxin reductase, and deiodinase.[29] It was demonstrated that, via enhancing glutathione excretion and production, sodium Se slowed the growth of Candida utilis. In mice, chitosan-functionalized SeNPs also increased glutathione peroxidase and predicted the development of lipofuscin. Additionally, using SeNPs in conjunct-tion with Cordyceps sinensis exopolysaccharide can scavenge superoxide anion radicals and ABTS°+.[30]

By using ABTS and DPPH tests, the plant-based production of Se NPs showed antioxidative activity. The Kong group also demonstrated the improved antioxidative activity of gum-arabic functionalized SeNPs (GA-SeNPs) for DPPH assay testing and hydroxyl radical scavenging.[20]

In one study, SeNPs reduced oxidative stress and improved liver function in rats, acting as a hepato-protective factor against acetaminophen's accelerated hepatotoxicity. The potential antioxidative qualities of SeNPs were shown. The literature has demonstrated that in these kinds of investigations, the size and form of the nanoparticles might be quite important. Hollow spherical SeNPs, for instance, have demonstrated antioxidative capabilities. Consequently, plant-based SeNPs provide superior protection against illnesses caused by oxidative stress and ROS. [31]

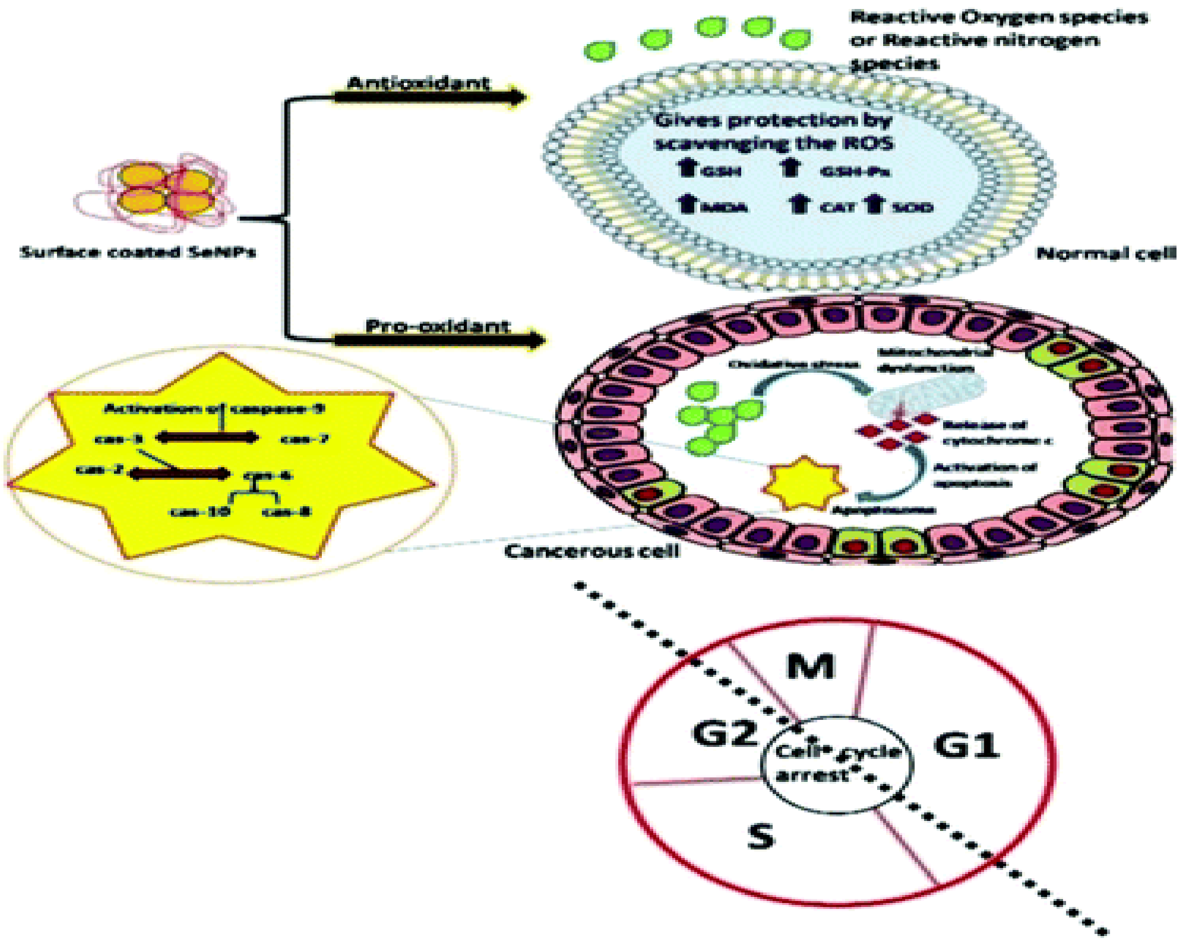

Figure 5: A systematic representation of the action mechanism by surface decorated SE-NPs on various cells as an antioxidant and a pro-oxidant with permission [31].

5-2- Antidiabetic activity

Chronic disorders like diabetes are brought on by the body producing too little insulin or using it insufficiently, which results in an excess of glucose in the blood. The substance known as insulin is in charge of preserving blood sugar levels. People of all ages are negatively impacted by diabetes. Due to their effective blood sugar-regulating properties, SeNPs have been used in the treatment of diabetes in several studies.

The long-term effects of diabetes can damage small and large blood vessels, which can affect how many human organs function. After eating, several disorders that impact the digestive system, immune system, brain, eyes, kidneys, skin, heart, legs, and teeth are brought on in a controlled manner and exhibit exceptional stability [31]. Cai L, Zhou S, Yu B, Zhou E, Zheng Y, Ahmed NSI, et al. investigated the enhanced anti-diabetic impact of Catathelesma ventricosum polysaccharides coated SeNPs using streptozocin (STZ)-induced diabetic rats. Similarly, the effect of insulin with SeNPs was investigated to enhance the activity of hyperglycemia and hyperlipidemia in mice with diabetes produced by STZ [24]. Utilizing chitosan-stabilized SeNPs at a dosage of 2.0 mg kg−1 body weight resulted in improved antidiabetic effect. Furthermore, studies on phytomedicines have shown promise in the treatment of diabetes [24].

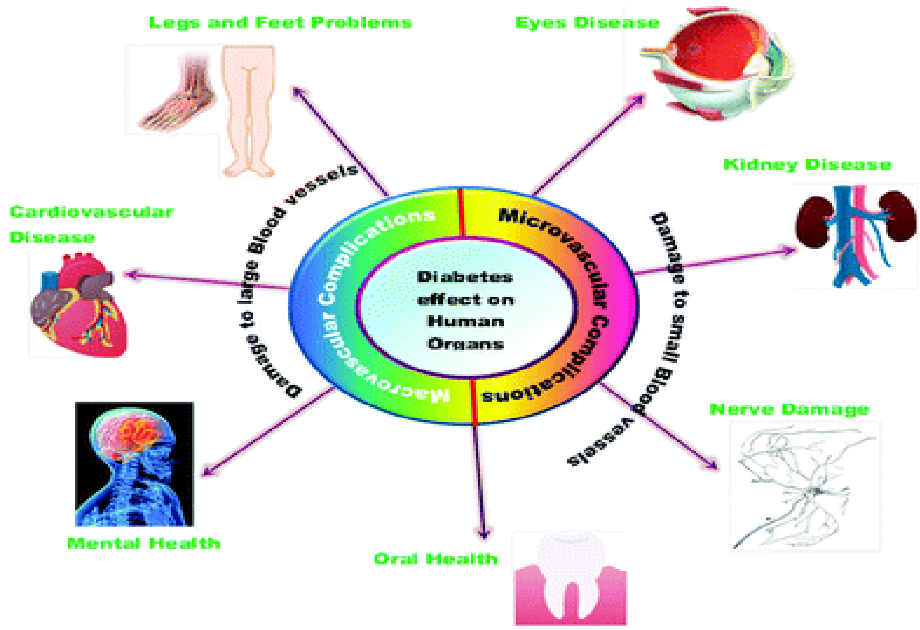

Figure 6: Effect of diabetes on various human organs (31)

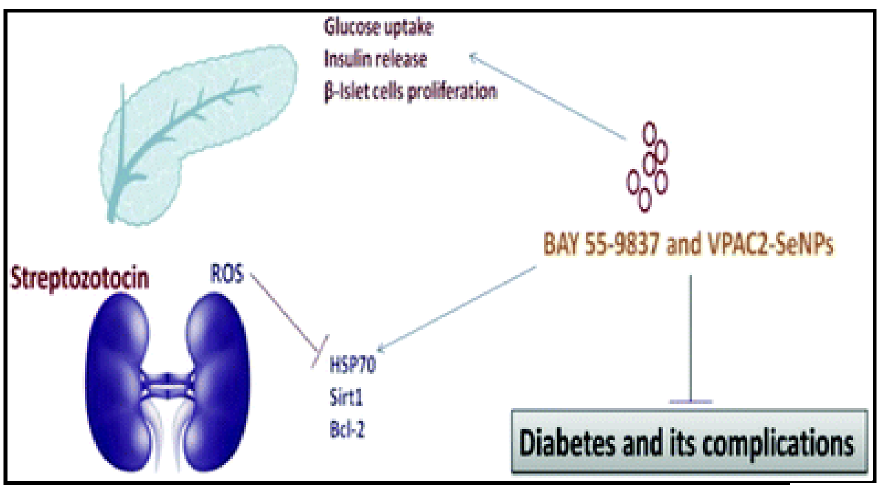

Figure 7: The effect of SeNPs on diabetic cells. Reproduced from ref stability (31)

6-Implications:

Many enzymes, including GPX and Se-containing proteins and molecules, are vital components of the body and include Se. Animals that are deficient in this element are more vulnerable to harm from specific forms of oxidative stress. In addition to improving targeting, increasing bioactivity, and lowering toxicity, nanoparticles also offer a variety of ways to control the release of the encapsulated moiety. Because of their significance at the cellular and tissue levels, researchers from all over the world have expressed interest in the biological uses of SeNPs. It is commonly known that several abiotic stresses can cause an excessive amount of hazardous (ROS), which can then lead to several disorders.

7- Conclusion:

SeNPs are considered a promising new era in several medical applications, as they have biomedical and pharmaceutical uses due to their antioxidant, antimicrobial, antidiabetic, and anticancer effects.

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