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RECENT ADVANCES IN SELENIUM CONJUGATED NANOPARTICLES

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ABSTRACT The welfare of people, animals, and microorganisms depends on selenium, a trace micronutrient. A lot of researchers have recently become interested in selenium conjuagted nanoparticles (SeNPs) because of their biocompatibility, bioavailability, and minimal toxicity. Consequently, selenium nanoparticles are widely used in a variety of biomedical uses due to their higher bioactivity. In general, physical, pharmacological, and biological techniques can be used to create selenium conjugated nanoparticles. The biologically produced SeNPs, however, show improved compatibility with human systems and tissues. Numerous researchers have looked into how their applications in biological systems are affected by their size, shape, and technique of synthesis. This review talks abouth the origin of selenium nanoparticles and also emphasises their uses in the biomedical field and discusses the various synthesis techniques used to prepare them. This review also talks about the various selenium conjugated nanoparticles being applied in the treatment of diseases.

KEYWORDS : Selenium , Biocompatibility , Synthesis , Techniques

Introduction

In the sciences of physics, chemistry, and biology, the element selenium (Se) is crucial. Selenium is naturally found in two different forms: inorganic (selenite and selenate) and biological (selenomethionine and selenocysteine).(Rayman, 2000) In nature, selenium can be found in both crystalline and amorphous polymorphic forms. The crystalline types of selenium are monoclinic and trigonal. Se8 ring-containing monoclinic selenium (m-Se) is crimson in colour. It exists in three allotropic versions (,, and) based on various packings.(Varlamova et al., 2021) Because of its low melting point and strong photoconductivity, it has excellent catalytic activity for organic hydration and oxidation reactions. Ideally it is suggested by doctors to have an intake of 60 and 70 grammes daily for men and women respectively pertaining to selenium .

Selenium is an important biochemical component. It is frequently used in dietary additives and may be a nutrient in fertilisers. (Gudkov et al., 2020)A diet deficient in selenium causes the liver and hemolytic systems to malfunction. Numerous illnesses, including Kashin-Beck disease, neurological problems, and chronic degenerative diseases, are caused by se deficiency. Supplementing with selenium can fend off illnesses like viral infections, impaired immune function, and loss of brain function. (Zafar et al., 2003) Metal nanoparticles have countless uses in biomedicine thanks to the recent growth in nanotechnology. The recent rise in nanotechnology offered an endless number of uses of metal nanoparticles in biomedicine. (Look et al., 1997)). The synergistic antibacterial activity of SeNPs and lysozymes was revealed by Vahdati et al. in study (Vahdati & Tohidi Moghadam, 2020) The surface of the particles is more exposed in the nanoscale because to their greater surface-to-volume ratio, which increases selenium activity more significantly in the nano-regime.

In biological applications, SeNPs exhibit promising potential as antioxidants, cancer therapeutics, and drug carriers. (Forootanfar et al., 2014)Their anticancer, antioxidant, antimicrobial, anti-biofilm, and anti-cancer effects have all been supported by several research. The treatment of Huntington's disease with nano-Se medication has produced encouraging results. (Cong et al., 2019)SeNPs are utilised in photocells, photocopying, photometers, and xerography and have special semiconducting, photoelectric, and X-ray sensing capabilities.(Shakibaie et al., 2015) Their significance in renewable energy equipment has also received considerable attention. Selenium nanoparticles (SeNPs) are also significant for the environment due to their capacity to capture mercury.

Synthesis of selenium nanoparticles

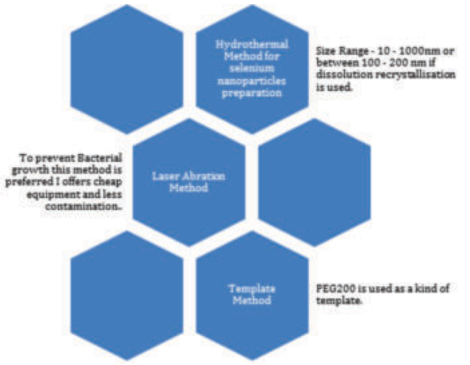

Fig 1 – Synthesis (SeNPs)

Hydrothermal Method for selenium nanoparticles preparation

By Niu et al., the hydrothermal synthesis was created with certain benefits including affordable, straightforward, and effective synthesis of crystalline selenium nanostructures.In a vessel containing deionized water , GeSe3 bulk glass that has been optically polished is typically put.(Pi et al., 2017)After this arrangement at the reaction temperature , the mixture gets hydrolysed due to which a colloidal suspension of amorphous selenium is created. So, SeNPs ranging from 10 to 1000 nm can be produced using this hydrothermal technique.(Srivastava & Mukhopadhyay, 2015)

Laser Abration Method for Selenium Nanoparticles

With the help of laser, the selenium pellet of a microcentrifuge tube was irradiated. This was generated by Guisbiers et al. to prevent bacterial growth. The laser beam was directed towards the target site with the idea of high repetition rate and shorter durations.. (Quintana et al., 2002)A 355 nm wavelength and a set 15 minute irradiation duration were used to create a more stable colloidal solution. In comparison to alternative approaches, laser ablation offers various benefits, such as a decrease in chemical reagent contamination and inexpensive equipment .(Jarvis & Martone, 1992)

Selenium Nanoparticles prepared by Template Method

With the aid of several chemical templates acting as stabilisers, selenium NPs can be created from selenium elements. (Zheng et al., 2012). Gray Se was first dissolved in a PEG200 solution at 210–220°C for 15–20 min, then water was added in a 1:1 ratio. The monodisperse and homogeneous spherical structures had an average diameter of roughly 5 nm. The template approach, which is based on chemical reductions, is most frequently utilised. Sulfate polysaccharides (SPS) were developed by Hu et al. as a template for the one-step preparation of Se NPs (S. Hu et al., 2020). To increase the solubility of the polysaccharides, they were dissolved in DMSO and agitated all night at room temperature. The SPS was then prepared by adding sulphur trioxide-trimethylamine (STMA) at a certain temperature. After being brought to room temperature, the resulting solution was neutralised .At room temperature, a 4:1 molar solution of sodium selenite and ascorbic acid was added to the produced SPS solution. At the end reaction result produced SPS – Se NPs.(Shin et al., 2007)

Drug Delivery By Selenium Nanoparticles

Functional nanosystems offer new therapeutic approaches for the treatment of disease by combining the benefits of regulated drug release and targeted drug delivery.(Liu et al., 2012; Shin et al., 2007) Se NPs demonstrated stronger selectivity to cancer cells as compared to individual drugs, as well as higher bioactivity, drug solubility, and targeting effects, which ultimately led to higher medication efficacy and fewer adverse effects. Galactose (GA) modified Se NPs were used by Xia et al. as an active tumor-targeting doxorubicin (DOX) delivery method.(18) Liu et al. created 5-fluorouracil surface-functionalized selenium nanoparticles (5FU-Se NPs), which greatly increased anticancer efficacy by inducing caspase-dependent apoptosis, in order to lessen the negative effects of chemotherapy medications. Sorafenib (SOR) has been loaded into an injectable Se NPs nanosystem by Zhang et al. that works as an efficient drug release library for both in vitro and in vivo tumour suppression. (Liu et al., 2012)

Immunomodulation Of Selenium Conjugated Nanoparticles

Immunotherapy has become a promising new method of treating malignant tumours. Se NPs have been demonstrated to boost immune therapy of tumours by taking advantage of the advantage to strengthen the anti-tumor cytotoxicity of immune cells. In order to activate anti-tumor immunity, Wang et al. created a new immunogenic core-shell Au@Se NPs by combining chemotherapy with photothermal therapy using Se NPs (J. Wang et al., 2020). According to the in vivo data, Au@ Se NPs not only produced anti-tumor immune responses with great cancer-killing effects when tumor-associated antigens were present, but they also successfully changed the phenotype of tumor-associated macrophages (TAMs) from M2 to M1. These outcomes might encourage T cell activation for tumour rejection even more, which would help with phagocytosis of the distant tumour. As infectious diseases are almost always accompanied by a variety of immunological reactions, it is possible to treat them by modifying immunity. Zebrafish have shown increased immunity and illness resistance to the bacterium Aeromonas hydrophila infection when fed dietary chitosan-selenium nanoparticle (CTS-Se NP). Zebrafish splenocytes showed increased proliferation following CTS-Se NP treatment with lipopolysaccharide (LPS) and concanavalin A (ConA) stimulation. Also, it was discovered that the up-regulation in IL-2 and IL-12 production was related to the immunological response of splenocytes against ConA.(Y. Hu et al., 2019)

Antiviral And Antimicrobial Activity of Selenium Conjugated Nanoparticles

Se NPs' potent antibacterial action has generated a lot of interest. Se NPs have the potential to replace antibiotics due to their greater ability to release selenium ions, which can be used to disrupt the structure of bacteria and prevent the development of multidrug-resistant diseases . (Lin et al., 2019) (Lara et al., 2018). Se NPs' antiviral properties were further demonstrated by their ability to successfully inhibit the proliferation of type-1 dengue virus when they were biosynthesized. (Li et al., 2011)

Protective Effects Of Selenium Conjugated Nanoparticles

Rezvanfar et al., for example, discovered that Se NPs' antioxidant activity may help to reduce cisplatin-induced gonadotoxicity. (Rezvanfar et al., 2013) Also, treatment with Se NPs greatly decreased the toxicity of cisplatin by reducing the damage to spermatic DNA and free radical toxic stress caused by cisplatin in male rats. The use of Se NPs to increase antioxidant activity and combat cisplatin-induced nephrotoxicity was also introduced by Li et al., demonstrating the intriguing potential of Se NPs in the protection of cisplatin-induced kidney injury . These studies imply that Se NPs may also function as a type of protective agent in chemotherapy to lessen adverse effects, which may offer new remedies for the present severe side effects of antibiotics used to treat infectious infections.

Anti – Bacterial Activity

Although most bacteria are innocuous and some even aid in digestion, the destruction of disease-causing germs, the battle against cancer cells, and the provision of important nutrients, bacteria are tiny organisms that have the ability to infect the body. A tiny percentage of dangerous bacteria can, however, displace good bacteria, which results in detrimental effects. Despite the fact that the majority of bacterial pathogens can be effectively handled by modern antibiotics, some exceptionally shrewd microorganisms or bacteria that are drug-resistant continue to pose a substantial threat to human health. Se NPs are a viable contender as antibacterial agents or chemosensitizers for enhanced immunotherapy because they can prevent a panel of nosocomial infections caused by harmful bacteria.(Hariharan et al., 2012)

Anti – Fungi Activity Of Selenium Conjugated Nanoparticles

Fungi pose a hazard to human health because they can infect different sections of different species' bodies. According to Mathé and Van Dijck (2013), the pathogen can be protected by its biofilms, which are covered in an exopolymeric material or extracellular polymeric substance matrix, from harmful environmental factors, fungicides, and host immunity.(Mathé & Van Dijck, 2013)Se NPs' potential impacts and mechanism for suppressing Candida albicans biofilms were studied by Guisbiers et al. At low Se NPs dosage, Candida albicans biofilm was 50% suppressed after Se NPs attached to the biofilm, penetrated into the pathogen, and subsequently disrupted the cell structure by substituting with sulphur.(Guisbiers et al., 2017)

Potential Application of Selenium Conjugated Nanoparticles in COVID – 19 Pandemic

For epidemiological research and the prevention of the COVID-19 outbreak, point-of-care testing for the disease are crucial.(Z. Wang et al., 2020) It's quite intriguing since cure rates have been discovered to significantly correlate with selenium intake levels in some locations, which raises the possibility that selenium may be used to treat COVID-19. Also, it has been demonstrated that organic selenium species can effectively inhibit COVID-19-infected Vero cells by covalently attaching to the COVID-19 virion Mpro via cell membranes (Jin et al., 2020)These can also be used as innovative anti-viral drugs to treat COVID-19 because to their capacity to inhibit various viruses and enhance innate and acquired immunity. There are, however, only few studies examining the antiviral effects of Se NPs against COVID-19; additional research is required to establish the function of Se Nps.

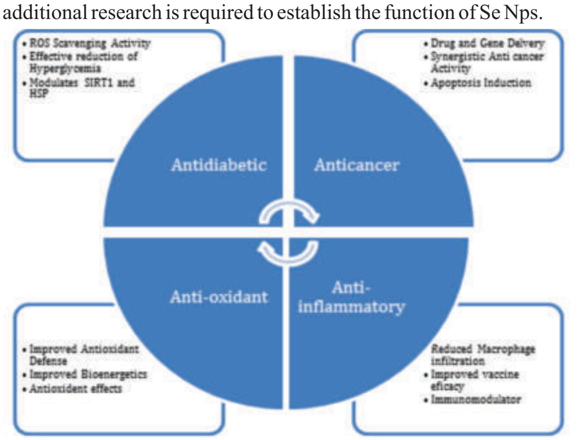

Fig 2 - Therapeutic Applications Of Selenium Conjugated Nanoparticles

Origin and Relevance Of NanoSelenium

The complicated problems associated with conventional medication forms and their dose forms are taken into account by nanomedicine-based techniques as possible solutions. The improved safety of nanomedicine is a well acknowledged benefit.(Chaudhary et al., 2014) SeNPs can be created using a variety of techniques, such as biological or synthetic onesSe is a crucial component of several selenoenzymes, including GPXs, TXNRDS, and deiodinases (DIO), all of which are necessary for the physiological antioxidant defence system (Regina et al., 2016)(Fernandes & Gandin, 2015). In a rat model, the application of SeNPs significantly lowers the death caused by acute toxicity associated with Se by up to four times (Jin et al., 2020). Furthermore, utilising SeNPs significantly lessens the liver damage brought on by high doses of Se, as shown by hepatotoxic biomarkers (H. Wang et al.,

2007) (Kumar et al., 2014) (Y. Huang et al., 2013)In vitro, SeNPs scavenge free radicals in a manner that depends on their size (5 nm–200 nm). Small (5–15 nm) SeNPs have a superior capacity to scavenge free radicals and prevent the oxidation of DNA, according to research by Bo Huang and colleagues.(B. Huang et al., 2003) Biological activity and bioavailability of SeNPs are superior to those of inorganic and organic Se molecules. Yet, SeNPs' fundamental flaw is poor cellular uptake. The outer surface of nanoparticles have been conjugated with targeted ligands in significant efforts to solve this issue. This offers an advantageous framework for cancer treatment. It has been demonstrated that adding amphoteric ligands, like polyethylene glycol (PEG), greatly aids in the creation of nanoparticles.

Different Types Of Selenium Conjugated nanoparticles and its recent advances

1. Synthesis of silymarin–selenium nanoparticle conjugate

To improve Sil's bioavailability, silymarin (Sil) was coupled to selenium nanoparticles (SeNPs). The native SeNPs had an average diameter of 20–50–1.5 nm, but the conjugates had a diameter of 30–50–0.5 nm. (Vargas-Mendoza et al., 2014) The conjugates were monodisperse. The MH-22a, EPNT-5, HeLa, Hep-2, and SPEV-2 cell lines were used to test the utilisation of SeNPs to boost the bioavailability of Sil. (Loguercio & Festi, 2011)When compared to the conjugate-free control, the EPNT-5 (glioblastoma) cells were the most responsive to the conjugates. The conjugates facilitated Sil's entry into the intracellular space and boosted the activity of cellular dehydrogenases. It's possible that SeNPs are primarily responsible for Sil's ability to penetrate cells, and that this ability is unrelated to phagocytosis.(Staroverov et al., 2021)

2. Sulforaphane-conjugated SeNPs: towards a synergistic anticancer effect

By the reduction of selenite with ascorbic acid, sulforaphane-modified selenium nanoparticles can be created in an easy aqueous-phase redox process. Sulforaphane molecules in the reaction mixture produce an adlayer by adhering to the surface of the nanoparticle. Many physicochemical methods, including microscopy, spectroscopy, x-ray diffraction, dynamic light scattering, and zeta potential tests, were used to evaluate the resultant conjugate. The nanomaterial administered intraperitoneally is mostly eliminated in urine (and, to a lesser extent, in faeces), as demonstrated in in vivo studies on rats, but it is also retained in the body. The modified nanoparticles predominantly collect in the liver, but the basic characteristics of blood and urine stay within normal ranges. The sulforaphane-conjugated nanoparticles exhibit significant anticancer activity (Krug et al., 2019)

Conclusion

Many hazardous illnesses, including cancer, neurological, muscular, immunological, etc., are caused by selenium deficiency. Due to its shortage, physiological effect, and toxic levels, selenium can typically only be shown within a very small concentration range. Se exhibits pro-oxidant action at higher concentrations while acting as an antioxidant at optimal doses. A precisely controlled dose of Se is typically advised to address this problem. Due to its bioavailability in the form of selenoproteins and decreased molecular weight, selenium provides a number of health benefits. Several selenoproteins, including glutathione peroxidases, thioredoxin reductases, and Se1P, Se1F, Se1S, and Se1M, exhibit redox activity and regulate redox processes in cells. Due to their connection with numerous moieties, including selenoproteins, selenocysteine, selenomethionine, etc., The toxicity caused by nanoparticles is still a serious concern for scientists, though. According to the research, the majority of SeNPs with a size between 50 and 200 nm were useful as therapeutic agents for treating cancer as well as for antioxidant and antibacterial applications. Selenium Conjugated nanoparticles have the potential to be used in dietary supplements and pharmaceutical applications in the near future. Biogenic SeNPs can be investigated for their potential as catalysts, drug delivery systems, and anti-TB and anti-viral agents. In particular, the development of new nanoparticle delivery systems can offer significant dietary and therapeutic potential by allowing selenium to be transported in organs, which can change the physiochemical properties of the nanoparticles.

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