Nucleus (2020) 63:107–118
https://doi.org/10.1007/s13237-019-00306-y

REVIEW ARTICLE

Use of selenium as micronutrients and for future anticancer drug: a review

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Received: 10 October 2019 / Accepted: 8 December 2019 / Published online: 16 December 2019

Abstract
The inherent duality of selenium can be the stepping stone to generate selenium based front line chemotherapeutic drug against ever evolving disease landscape of cancer. Not only as a therapeutic agent, but also in supportive care this essential micronutrient may be a good supplement to balance redox homeostasis and boost up patients immunity. Many in vitro, in vivo and clinical studies have generated a lot of useful information about anticancer properties of this trace element, which can be used as backbone in these aspects. The knowledge about speciation, distribution and compartmentalization of selenium metabolites, their pharmacokinetics, regulation of selenogenome and selenoproteome function, genomic variants and epigenetic effects are to be integrated to achieve the novel target. Advancement of bioinformatics and new technologies can be very much helpful in this regard.

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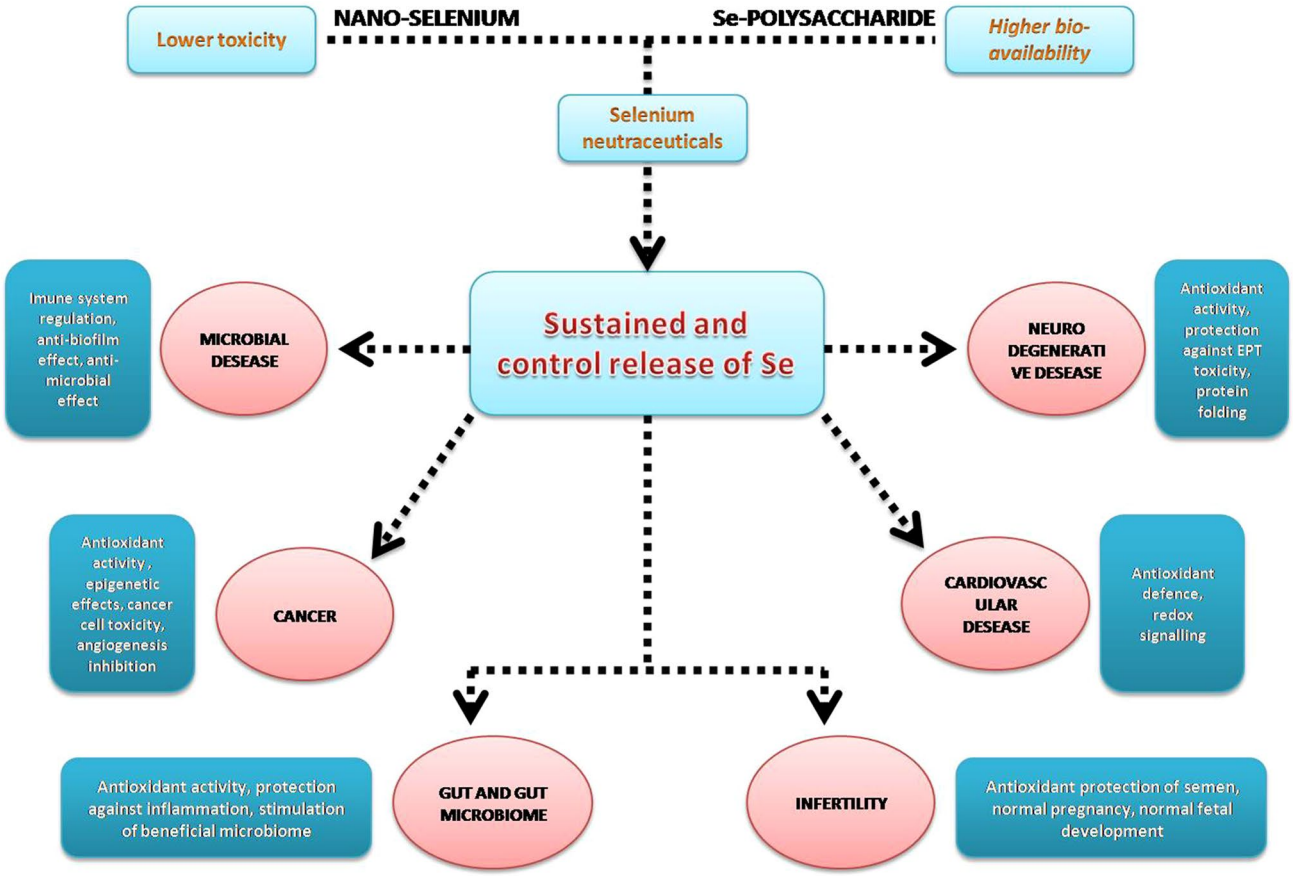
Graphic abstract



Keywords Cancer · Chemotherapy · Immunity · Omics · Redox biology · Selenium

Introduction

Duality is the inbuilt characteristics of the trace element selenium ($^{78.97}Se_{34}$). This metalloid was successfully named after 'selene', the Greek name for the moon; because selenium has dark side and bright side just like two faces of moon. Initially after its discovery in 1817, it was considered as toxic chemical but after 200 years, it is now recognized as an essential micronutrient with numerous health benefits for human. Research efforts of previous century were focused mainly on the chemopreventive potential of various selenium (Se) compounds against cancer. Although the findings of these studies are conflicting, a lot of knowledge was gained about seleno compounds and selenoproteome. Maintenance of cellular redox homeostasis is very much dependent on cellular selenoproteome, which is indirectly dependent on supplementation of Se. Integration of Se in redox biology starts with the translation of 21st amino acid selenocysteine that uses the codon degeneracy like property of opal stop codon (UGA), suitable with the dual nature of Se. Selenoproteins encoded by 25 separate human genes perform cell protection from oxidative stress, redox control, and the inflammatory response. Se-dependent glutathione peroxidases and thioredoxin reductases are necessary for optimal function of immune cells by controlling oxidative stress and redox regulation. As selenoproteins, act principally as antioxidant, but research findings of previous century undoubtedly proved the prooxidant character of various seleno compounds, that is why it is a master regulator of cellular redox balance with its remarkable duality. Different Se compounds are reported to augment the therapeutic efficacy of standard anticancer drugs and efforts are on the way to generate Se compounds as front line anticancer agents that needs special attention to the ever increasing incidence of cancer.

It is well known that cancer cells undergo uncontrolled cell division and proliferation. In order to support this phenomenon, cancer cells undergo aberrant metabolic adaptation as well as to counteract the enhanced oxidative environment due to aberrant metabolism. Cancer cells utilize the cells' antioxidant scavenging systems for survival. As a

result cancer cells fail to further adapt to any additional oxidative burst by any process. Even a slight induction of ROS makes the cancer cells vulnerable resulting oxidative stress-induced cell death. On the other hand normal healthy cells have steady supply of antioxidant enzymes and low level of ROS. If by any reason the ROS level is increased, it is counteracted by the antioxidant defense system and a steady state is maintained. If the ROS level can be enhanced or the depleted antioxidant defense system is targeted to a threshold level which is incompatible with cancer cell viability, then it is possible to kill cancer cells without affecting the normal healthy cells. Use of small molecule redox modulator provides a therapeutic window and can be applied for a successful anticancer therapy.

Se compounds have been well established as redox modulator with antioxidant as well as pro oxidant properties and highly specific towards cancer cells in terms of cellular uptake, localization and accumulation in cancer cells. This uptake mechanism differs between different Se compounds and is not clearly understood. Hence, Se compounds with its pro oxidant character offers a promising candidate for successful anticancer therapy. At the same time its antioxidant properties will confer protection to the normal cells. Generally inorganic Se compounds impart high genotoxicity resulting higher systemic toxicity which may account for lower therapeutic window. On the other hand organo- Se compounds show significant antitumor activity with less systemic toxicity, and enhanced bioavailability with fewer side effects. Organo Se compounds are nucleophilic molecules with diverse nature. Several organic -Se compounds are being synthesized with a view to improve the selectivity, specificity at the same time with lower toxicity and due to these improved properties organo Se compounds are becoming promising candidates for cancer therapy. Nano selenium has recently been emerged as a novel agent to combat cancer due to its bioavailabilty, selectivity and low toxicity [5]. Biogenic Se nano particles are being synthesized using different techniques for therapeutic purpose. Its anticancer effect is exerted directly and as drug delivery system.

Nutritional need of selenium

Much of the knowledge about the nutritional role and requirements of selenium in human was gained from various chemopreventive studies, different disease conditions and from the consequences of toxic selenium exposure. Although, selenium in inorganic form failed to prevent prostate cancer risk in SELECT (Selenium and Vitamin E Cancer Prevention) trial, encouraging results using organoselenium compounds against carcinogen induced challenge are also reported. Diphenylmethyl selenocyanate was found to prevent DMBA-croton oil induced skin carcinogenesis [17, 18], benzo (a) pyrene—lung carcinogenesis [19] and azoxymethane induced colon carcinogenesis [35]. Despite its organic or inorganic form, high dose of Se was used as chemopreventive agent [24, 80], often exerting various detrimental effects [59]. Se compounds which cannot synthesize Se dependent enzymes still poses cancer chemopreventive properties, suggesting different anti carcinogenic mechanisms [34]. Due to the narrow window between beneficial and toxic dose of Se [78], design and synthesis of different organoselenium compounds for various purpose was taken into consideration. To name a few, a series of synthetic organoselenocyanate compounds with 1, 8-naphthalimide moiety showed effective antioxidative properties against 7,12-Dimethylbenz[a] anthracene [DMBA]- phorbol-12-myristate-13-acetate [PMA]-induced oxidative stress and cadmium induced redox imbalance [45, 46]. Spiro 6-methoxytetralin-1, 3'-pyrrolidine based organoselenocyanates was found to be effective against cadmium- induced free radical mediated hepatic injury [47]. Diphenylmethyl selenocyanate was also effective against cadmium- induced hepatotoxicity and malachite green induced oxidative damage [20, 21]. The antioxidative properties of these organoselenium compounds may be due to their ability to activate antioxidative defense machinery [80, 86]. Besides that, at low nutritional levels selenium can activate other low molecular weight antioxidants (Q10, vitamin C, E and others) [40]. However, brain function, male fertility, endocrine functions are among the few examples which are very much dependent on nutritional supply of Se [77, 85]. Se related health hazards are of two types arising from its deficiency and excess. Severe deficiency of Se resulted in two well known endemic diseases, Kashin–Beck and Keshan diseases [78]. Chronic and acute exposure to Se by inhalation can cause irritation of the respiratory tract and lungs, as well as cause bronchial spasms, headaches, pulmonary edema, symptoms of asphyxiation and persistent bronchitis, elevated pulse rates, lowered blood pressure, stomach pain, nausea and vomiting [78]. Selenosis is reported due to chronic and acute oral intake of Se [78]. Toxic effects of Se can also hamper the synthesis of thyroid and growth hormones; disrupt the endocrine function and metabolism of insulin like growth factor. Dietary Se at particularly high levels is also reported with significant impairment of natural killer cells and hepatic function [76]. Conventionally the term, "selenium" in basic science and nutrition research is used to denote different Se compounds without considering the fact that the toxic side effects of Se depend on its chemical form [41]. The burning example of potential misunderstanding are evident in current reference standard for Se intake (e.g., TDI or Tolerable Daily Intake, RDA or Recommended Dietary Allowance, LOEL or Lowest Observed Adverse Effect and NOAEL or No Observed Adverse Effect Level), where values are given without any specification of its chemical form. The effect of Se is also concentration

dependent, ranging from essential as antioxidant to potential prooxidant at an toxic level [71]. World Health Organization (WHO/FAO/IAEA, 1996) recommended daily dietary requirement of selenium as 21 µg for men and 16 µg for women [20] whereas the maximum allowable concentration (MCL) in drinking water is to be 50 ppb (0.05 mg/l) [98]. The relationship between Se status in the body and health effects is U-shaped implying that super nutritional intake may benefit people with low Se status whereas those with adequate-to-high status might be affected adversely [77]. So, these matters are of particular concern during the daily nutritional requirement and its use as a supplement for any kind (Fig. 1).

Present knowledge of selenium biology

Selenium in various forms is found in nature ranging from elemental isotopes to cellular proteins. Selenocysteine (Sec) containing selenoproteins are most common and best studied among selenoproteome family, whose translation depends on duality of UGA codon [5] due to property like codon degeneracy. At present, more than fifty selenoprotein families are known among all domains of life (bacteria, archaea and eukaryotes) with new discoveries adding up. Despite this widespread presence, distribution of selenoprotein families varies from zero (fungi, higher plants, beetles, silkworms etc.) to 1 (*Caenorhabditis elegans*) and even up to 59 (*Aureococcus anophagefferens*) indicating evolutionary trend of low to high selenoproteome dependency in terrestrial versus aquatic life forms [57]. From in silico analyses, the number of genes encoding selenoproteins in mouse and humans are found to be 24 and 25 respectively [56]. In humans, 25 genes encode 17 selenoprotein families (5 forms of glutathione peroxidase or GP*x*s, 3 forms of thioredoxin reductases or TrxR and 3 forms of iodothyronine deiodinases or DIOs), amongst which three selenoproteins, TrxR1, TrxR2, and GP*x*4, are found to be essential for life [71]. Structurally mammalian selenoproteins are of two kinds depending upon the position of Sec—(i) Sec at C terminus, such as TrxRs and selenoproteins S, R, O, I, and K, (ii) Sec at N terminus, including GP*x*s, DIOs, selenoproteins H, M, N, T, V, and W; SPS2, and Sep15 [63]. Functionally, mammalian Se containing proteins are of three types, (i) Sec containing selenoenzymes, (ii) selenomethionine (Se-Met) containing selenoproteins and (iii) Se binding proteins (SBPs) [99]. Se binding proteins (SBPs) are of very small family amongst which SBP1 is required for intra golgi transport and protein degradation [25]. SBP1 expression is a

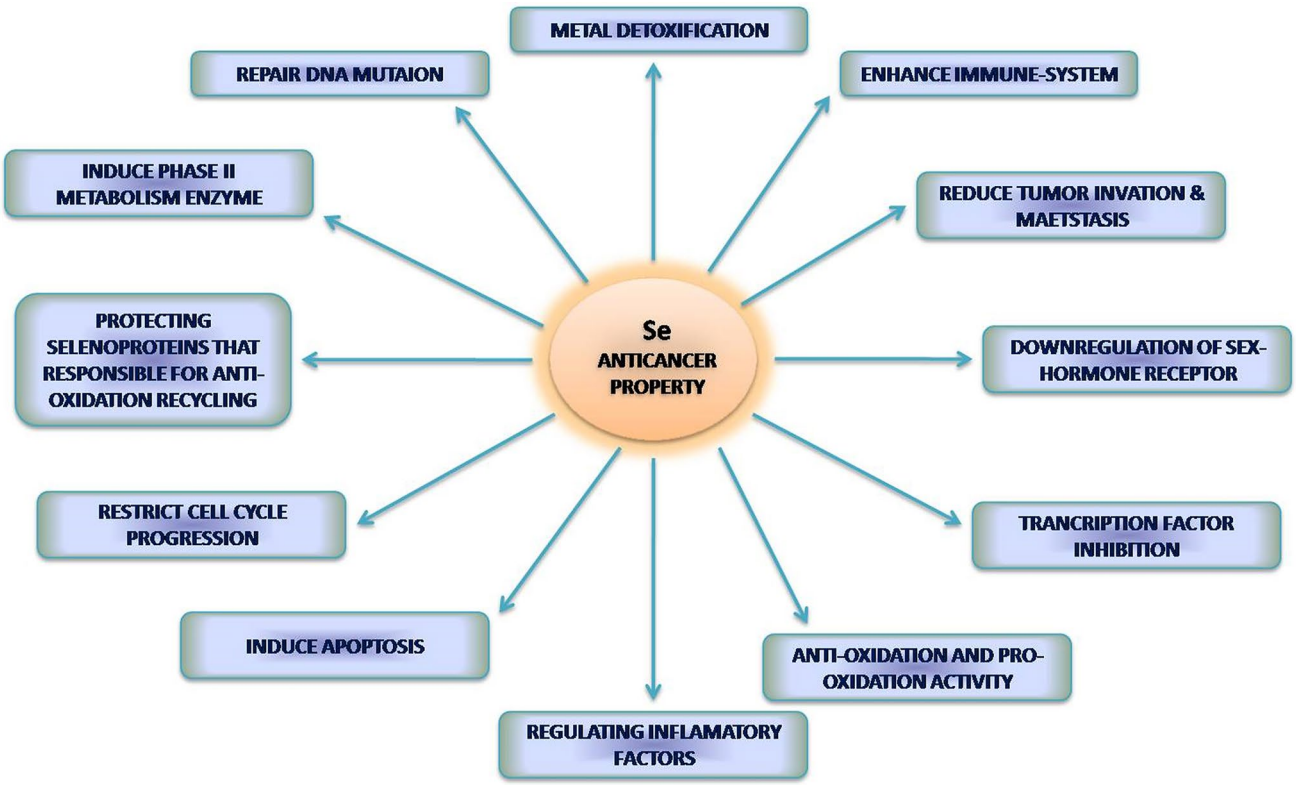


Fig. 1 The role of selenium in biological systems

reported marker for cancer development and schizophrenia [25], which itself and its homolog SBP2 is suggested to function in detoxification [84]. Most of the selenoproteins with Sec in their active site are known for antioxidant properties like removal of hydroperoxide which is glutathione-dependent, reduction of thioredoxins, synthesis of selenophosphate, regulation of thyroid hormones, assembly of cytoskeleton, systemic transport of this trace element and protein degradation via endoplasmic reticulum. Reducing property is also evident among selenoprotein, MsrB1 (also known as SelR or SelX; a methionine sulfoxide reductases) that reduce methionine sulfoxides to methionine is essential for mammalian cytoskeleton assembly. Se-Met containing selenoproteins are formed via the replacement of Met by Se-Met which may provide protection against (i) free radical species to susceptible nearby amino acid residues and (ii) amyloid proteins and neurotoxicity. The detail account on the molecular weight, tissue distribution and subcellular locations of human selenoproteome, are elegantly reviwed by Roman et al. [78]. Selenoprotein P (SEPP1) which distributes Se from the liver can affect total Se status, male fertility and colon cancer [77] and Selenoprotein W (Se W) as an effective responder to stress is an effective antioxidant, essential for immunity and neuron development [29, 60].

The regulation of selenoprotein function depends on selenoprotein mRNA level [93, 99], cellular compartmentalization [16, 49, 61, 74], interactions among themselves [5], and the nature of selenocompounds provided as supplementation. It is worth mentioning that naphthalimide based organoselenium compounds are found to activate phase II detoxifying enzymes [80]. Transport of Se is another aspect to be considered for synthesis of biomedicine [54], because distribution of Se depends on essentiality [7] and life forms [67, 79] which is helpful in the synthesis of selenocompounds for supplementation (Fig. 2).

Rationale for selenium supplementation during cancer care

The role of Se deficiency on the overall health condition of normal individual is discussed in previous section. Reduced Se levels are found in smokers with advanced age and the mechanism is not yet completely understood. Consumption of eggs, white rice, alcohol, and coffee is also associated with Se depletion [72]. Incidence of various diseases,

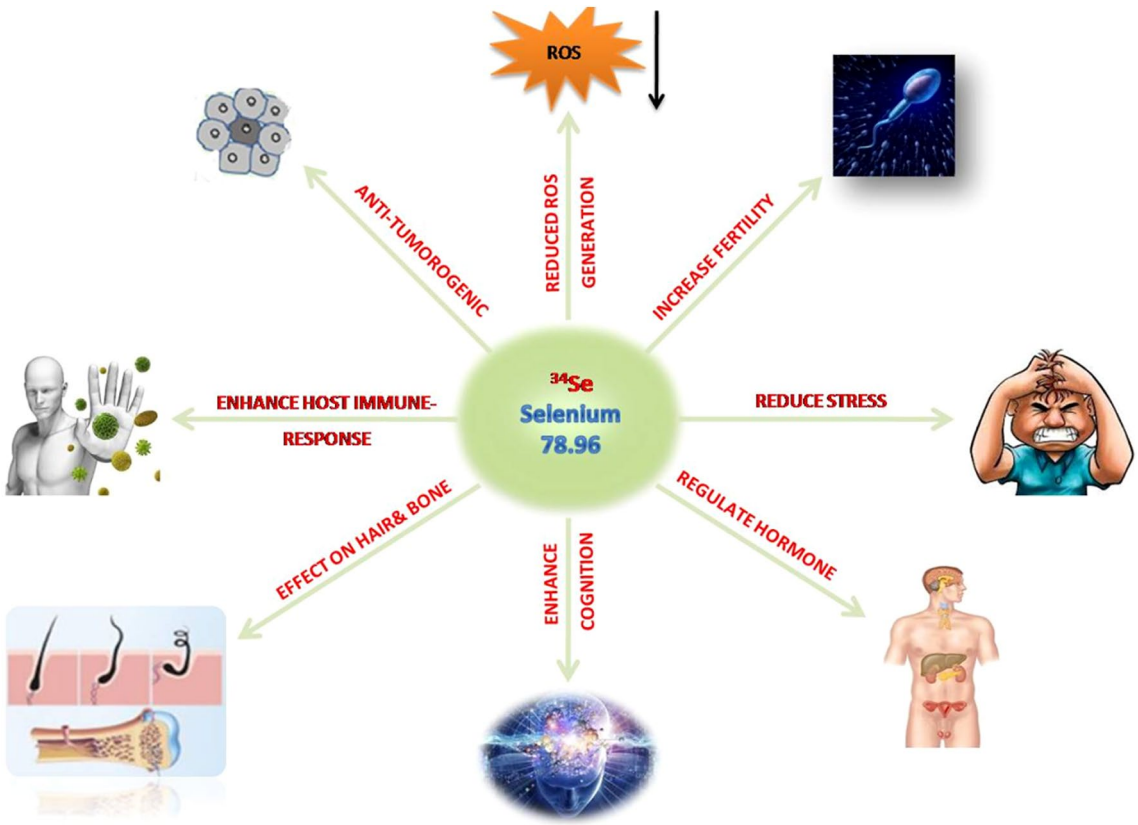


Fig. 2 Principle effects of the selenium on human physiological system

particularly cancer is another cause of Se deficiency [32]. Chemotherapy and radiation along with suboptimal nutrition in patients especially from developed and underdeveloped countries can aggravate the condition of a Se deficient patient even further that increase the side effects during and after therapy [8, 67]. Quality of life of cancer patient can be improved by Se supplementation at daily dosage level of 2000 µg either alone or along with vitamins [8, 67, 68]. So, synthetic Se compounds are the only way for supplementation to get the best effect of this trace element [64, 65]. Considering that the organic form has better absorption, it seems to be the preferable formulation for supplementation or treatment [94]. Se as a micronutrient is well documented for effective chemoprotection [23]. Diphenylmethyl selenocyanate showed nephroprotective activity against cisplatin [12]. Naphthalimide-based organoselenium compounds were found to be myeloprotective against cyclophosphamide and nephroprotective against cisplatin [36, 81]. A coumarin based synthetic organoselenium compound was found to be effective myeloprotectant against carboplatin [73]. Different Se compounds are also being reported to induce and augment apoptotic cell death when given as adjuvant along with standard anticancer chemotherapeutic drugs [66]. To name a few, naphthalimide based organoselenium compound effectively enhanced the therapeutic activities of cyclophosphamide and cisplatin against in vivo breast cancer model [37, 82]. Flavonyl-thiazolidinedione based organoselenium, diphenylmethyl selenocyanate was also reported to sensitize cyclophosphamide therapy in vivo [13, 83].

Immune function is reported to be impaired during cancer and further compromised from chemotherapy indicating possibilities of different infection and disease [77]. Although the detailed precise mechanistic is needed to be found out, Se supplementation is reported to boost up immune function, which can be very crucial factor for ultimate therapeutic outcome against cancer [43, 77]. Although, relationship among Se and asthma was found to be inconsistent, a recent study by Polish group reported allergic role of Se from food especially in infants [42, 52]. Another cohort study from New Zealand with infants of similar age did not find such strong association between Se and allergy [95]. As numbers of child cancer are increasing globally, so this point is to be taken care of on emergency basis because cancer patients' lifespan and quality of life is very much dependent on Se in many ways.

Development of frontline anticancer selenium compound

The dual nature of Se (antioxidant and prooxidant) is not only evident in various Se compounds but it is also true for selenoproteins [87]. Genomic analyses have enriched the study of the Se biology with respect to the identification of selenoproteins in different domain of life, genetic variants associated with adaptations to their Se nutritional histories, and the association of specific genotypes with common and rare human Se disorders. Whether supplementation of Se can prevent the cancer risk might be a matter of debate but strong relationship between single-nucleotide polymorphisms (SNPs) in selenoprotein genes and cancer risk are available from various epidemiological studies. As specific RNA structures are needed during selenoprotein translation, so SNPs within the flanking 3′-UTR may alter particular selenoprotein expression. Genetic alterations in different selenoproteins like H, N, P, R, S, W, Sep15, GP*x*1-4 and TrxR1-3 are reported to produce functional variants. The GP*x*1 isoform (rs1050450), originated by substitution of proline instead of leucine, alter overall GP*x* activity and reported to be a risk factor for cancer of breast, bladder or lung [53, 76]. In GP*x*4, a particular SNP (T/C) instead of (C/C) at nucleotide position 718 is linked with adenocarcinomas [2]. A study among the population of the Czech Republic, showed significant association of three SNP with an altered risk of colorectal cancer: rs7579 (in selenoprotein P or SEPP1), rs713041(in glutathione peroxidase 4 or GP*x*4) and rs34713741 (in selenoprotein S or SELS) [63]. These evolutionary and association studies through advancement of bioinformatics contributed to the genomics of Se has opened a new era in Se therapeutics. Se not only modulates gene expression of chromosomal DNA, but also exerts its effect on mitochondrial DNA [22, 28]. Epigenetic study revealed that various Se compounds can impact methylation capacity which can alter global gene expression [91]. Additionally, Se has also found to alter histone modifications via inhibition of histone deacetylases (HDACs) activity by its metabolite seleno-α-keto acids [90]. So, these factors are to be tested before recommendation for any specific selenocompound as a frontline anticancer agent [92]. Another major hurdle to use selenium as a frontline anticancer drug is its delivery in redox active form in suitable way and proper route into the tumor [97]. As an effective anticancer nutrient, Se can modulate proliferation; inhibit angiogenesis and invasion [105]. Role of Se is also tested against metastasis with promising outcome in vivo [14, 99, 100, 103]. The effect of various Se compounds and the role of different selenoprotein on metastasis is reviewed in detail by Chen et al. [15]. Se is also reported to affect cancer stem cells in many ways [70]. But, Se in its naturally occurring inorganic (selenite) and organic form (selenomethionine) is not very suitable as a frontline anticancer agent [69]. Description of various synthetic Se compounds with their precise anticancer activities is elaborated by Zeng et al. [105]. Primarily they modulate redox homeostasis and signaling affecting metabolism and growth regulation which in turn alter differentiation, proliferation, senescence that ultimately leads towards cell death

pathways [1, 33, 50, 95]. The anticancer efficacy of various Se compounds is well established from many in vitro and in vivo studies, which are very specific depending upon structures and concentrations of the compound along with the particular experimental model which together influence bioavailability of test molecules, their reactivity and dynamics of action [2]. Structure activity relationship is also very crucial for its proper functioning because organic Se compounds are found to be very effective anticancer agents and their activity depend on particular carrier moiety [33] and chain length of methyl group attached [50, 80]. Molecular topology, surface area, volume and the bond order of the synthetic organoselenium compound are also to be considered for this purpose [31]. All these factors are to be considered in synthesizing Se- based frontline anticancer agent.

Present scenario and future possibilities

Supplementation with Se is reported to affect various biological processes in different manner depending on specific compound under investigation [58]. Therapeutic application of Se against cancer is dependent on various matters like target specificity, specific uptake etc. which are to be addressed with new technological tools and advancement of different interdisciplinary study arena [29]. To design suitable Se compound for frontline anticancer therapy, proper knowledge about speciation product after its supplementation is the first point to begin with. This is a major challenge in Se biology because nutritional source of Se is under continuous recycle due to incorporation and release of it during protein turnover. With the help of new chromatographic techniques like ICP-MS (inductively coupled plasma mass spectrometry) this speciation issue can be addressed [11, 48, 55] and was unravelled by Encinar et al. [27]. Oxidation artifacts can be another misleading issue during speciation study, because Sec and other selenols also undergo oxidation. Liquid chromatography time-of-flight mass spectrometry (LC-TOF-MS) enabled the detection of 103 selenized species as the selenometabolome of selenized yeast [38]. Such techniques increase the possibilities to find out the key metabolite of different Se compounds for various therapeutic purposes as potential clinical candidate. Distribution of Se source as various metabolite and protein in different cells and organ is another issue to be addressed. Majority of Se is found to be distributed only in plasma as selenoprotein P (SEPP1; 68 ± 7%), followed by glutathione peroxidase (GP*x*3; 25 ± 4%) and bound to serum albumin (7 ± 4%) [30]. A combination of XAS (X-ray absorption spectroscopy) and XFM (X-ray fluorescence microscopy) can help to link the speciation and distribution of Se to its biological activity in human lung cancer cells A549, demonstrating the distinct cellular fates of SeMet, MeSeCys and selenite [96]. This will help to generate Se based specific potential lead molecule against different stages of various cancer types. Compartmentalization of specific Se species is the next challenge to solve, because this issue can influence the levels of Se in serum as observed from supplementing SeMet and inorganic Se [9, 10]. Cancer is known to produce oxidative stress which is found to be associated with decrease of tissue Se concentrations [39]. While selecting selenium compounds for anticancer therapeutics the potential lead molecule should not interfere with Se homeostasis and the normal antioxidative defense system of patients. Use of nanotechnology may be another suitable option, as Se nanoparticles were reported to be effective chemoprotectant and chemosensitizer in vivo [3, 4, 6]. Different interdisciplinary factors are also involved regarding the use of selenium in anticancer therapy. As observed in vivo, disturbance in Se status can critically alter redox homeostasis in target tissues resulting in increased risk for pathogenesis of breast cancer [26]. Genotype of particular patient is another clinically critical checkpoint during application of Se containing anticancer drugs, because a very common polymorphism in Selenoprotein P gene (SELENOP) can markedly alter Se level in breast carcinoma [104]. At therapeutic dose, the pleiotropic effects of Se compounds are reported to modulate molecular markers of drug resistance expressed in cancer cells, the surrounding tumor micro environment and by cross-talk among them [51]. So, these factors should be considered before and during clinical trial of any particular Se compound along with the advance technology. Based on the data of translational research of RAPID Program (Rapid Access to Preventive Intervention Development by the National Cancer Institute) with Se-Methylselenocysteine (MSeC), the NOAEL value for humans was determined to be 7000 µg Se/day (for a 70 kg person) [62]. No conclusive result on the dose-toxicity relationship was obtained in a randomized and double-blinded study on the pharmacokinetics of MSeC [7]. Similar clinical trial with inorganic Se compound is also underway at various stages and is reported that supplementation of inorganic Se may be beneficial as adjuvant during radiotherapy [75]. Our working group has found synergistic anticancer activity of a coumarin based organoselenium compound along with carboplatin in human breast cancer cell line in vitro and the mechanism is underway in vivo [73]. A recent report of phase I clinical trial [88] on an organoselenium compound along with carboplatin and paclitaxel in cervical cancers is an impetus for us to proceed further with the synthesizing and formulation of organoselenium compound for clinical trial in near future [73].

Nanotechnology as an aid for modifications

Se in nanoparticle form may be a promising alternative to nutritional supplements or in oral drug delivery system. Incorporation of nanotechnology in nutrition is advantageous with respect to taste, smell, solubility,

administration, protection from oxidation and enzymatic degradation, prolonged residence time, and enhanced bioavailability [89].

Se in nanoform is advantageous due to its high bioavailability and low toxicity than its inorganic and organic variants. Se nanoparticles (SeNPs) of smaller size have greater biological activity with its possible use in zero oxidation state (Se^0), which is less toxic and highly bioavailable. But, it is unstable and easily transformed into inactive form [25], which can be solved by encapsulation. SeNPs has wide range of biomedical applications as an antioxidant, chemopreventive agent and anticancer drug delivery carrier. In addition it can be used against metal toxicity, as immunostimulant and other activity [89].

Anticancer effects of SeNPs: as direct acting agent or as carrier of anticancer drugs

SeNPs has direct anticancer activities. It can inhibit the growth of cancer cells through induction of cell cycle arrest at S phase by deregulation of the eIF3 protein complex for anticancer activity [44]. Treatment with SeNPs lowered the adhesion force and Young's modulus in cancer cells. Anticancer activity of SeNP is selective because of its unique internalization through endocytosis followed by apoptosis. Recently, nanoparticle form of Se (Nano-Se) has emerged as a highly effective agent in various aspects of cancer management, ranging from cancer chemoprevention to chemoprotection against chemotherapeutic drug-induced toxicity, and in potentiating in chemotherapy [3, 6]. SeNPs show better biological activity in comparison to other Se based compounds due to good adsorptive ability as a result of interaction between the nanoparticles and NH, C=O, COO–, and C–N groups of proteins present in the cell membrane. It has huge advantages such as greater surface area and reactivity, adequate gastric residence time and high permeability, and increased solubility in both hydrophilic and lipophilic phases. Another advantage of SeNPs is that it can be used in aqueous medium.

SeNPs are also efficient drug delivery agents due to its nano size and selective drug accumulation. Cancer cell specificity arises due to passive targeting process and encapsulated surface. Use of *Spirulina* polysaccharides (SPS) is a simple solution-phase method for functionalization of SeNPs which enhanced its uptake and cytotoxicity in vitro [101]. Folic acid-conjugated SeNPs (FA@SeNPs) was reported to sensitize radiation therapy [102].

Anticancer synergism was achieved by using 5-fluorouracil surface-functionalized SeNPs (5-FU-SeNPs) in vitro with selectivity towards cancer cells [62].

Market potential of SENP

Clinically used chemoprotective agents are very few and these are not also devoid of toxicities. Beside that these agents are costly. The chemosensitizing activities of Se compounds are well established in numerous studies [3, 6]. Various selenium compounds like selenate, ethaselen, L-selenomethionine are in clinical trials (phase I to phase III) for oxidative stress related disease including atherosclerosis, adenomatous polyp recurrence, different forms of cancers, thyroid diseases and others. However, post SELECT (Selenium and Vitamin E Cancer Prevention Trial) era is mainly concerned to mitigate the gap between the therapeutic efficacy and toxicity of the Se compounds since the gap between the safe dose and the toxic dose is very narrow.

Because of the potential antioxidant and prooxidant nature of Se, it offers a great probability to be used in combination cancer therapy with standard chemotherapeutic drugs. Se-containing nanoparticles (SeNPs) have recently garnered a great deal of attention as potential cancer therapeutic payloads, due to their excellent biological activities and low toxicity. Abundant evidence actually supports the better biocompatibility and bioefficacy of SeNPs when comparing to inorganic and organic Se compounds. A plethora of SeNPs has been developed in the last decade with the aim of obtaining new Se-based therapeutics and theranostics.

Conclusion

This review brings out the merits and demerits of Se and its different chemical forms and discusses the potential of nanoselenium as adjuvant in chemoprevention and therapy. Se being an essential micronutrient is required for optimal health and its deficiency is associated with health disorders like Kashin–Beck and Keshan diseases. Nutritional need of Se is manifested by the selenoproteome function essential for proper functioning of antioxidative defense system. Beside its daily requirement, Se is also essential in cancer care. Due to potential antioxidant and prooxidant nature of selenium, it offers a great probability to be used in combination cancer therapy with standard chemotherapeutic drugs. Advancement of new technology can be helpful for the development of Se based frontline anticancer therapy. Recently SeNPs have gained wide attention due to its low toxicity and excellent biological activities. Efficacy of SeNPs is better than inorganic and organic Se compounds. Thus various SeNPs have been synthesized with the aim to develop new Se-based therapy.

Acknowledgements ARP thanks University Grants Commission (UGC), New Delhi, India (18-12/2011(ii) EU-V) and SH acknowledges

Science and Engineering Research Board (SERB), Department of Science & Technology (DST), New Delhi, India (SB/YS/LS-121/2014) for their respective research grants. Authors also thank Director, Chittaranjan National Cancer Institute, Kolkata for providing infrastructural facilities.

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