UDC 636.087.72 http://dx.doi.org/10.15407/animbiol19.03.009

PERSPECTIVES OF CERIUM NANOPARTICLES USE IN AGRICULTURE

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In recent years, nanotechnology wins key positions in various fields of knowledge thanks to the special provisions with nanoparticles, namely their size and physicochemical properties. High ability of metal nanoparticles to accumulate leads to their accumulation in plant and animal organisms by increasing the bioavailability, overcoming biobarriers, tying together nucleic acids and proteins.

The accumulation features of nanoparticles of metals in plants, the impact on germination and vegetation, metabolism and productivity are researched in the article. Data on the use of metal nanoparticles in animal feed as an antibiotics alternative to increase productivity are analyzed. It is established that the rare earth elements may intensify the exchange of proteins and other nutrients by stimulating hormones activity inducing the synthesis of metallothioneins and growing conversion ratio feed. The changes of prooxidant-oxidant status of animal blood by the use of drugs with nanoparticles of cerium dioxide and changes of homeostasis are established. The use of rare earth elements is positive for poultry egg production because of egg production intensification, their weight and rate of fertilization of eggs for hatching. The influence of nanoparticles on metal redox potential and processes of lipid peroxidation in animals is established. Nanodispersed ceria use as a promising nanobiomaterial for biological and medical applications and the need for further research to study all possible mechanisms of its biological activity are argued.

Keywords: NANOPARTICLES, CERIUM DIOXIDE, BIOTRANSFORMATION, PRODUCTIVITY, REDOX PROCESSES

ПЕРСПЕКТИВИ ВИКОРИСТАННЯ НАНОЧАСТИНОК ЦЕРІЮ У СІЛЬСЬКОМУ ГОСПОДАРСТВІ

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В останні роки нанотехнології завойовують ключові позиції в різних галузях знань завдяки особливому положенню наночастинок за розміром та фізико-хімічними властивостями. Висока здатність наночастинок металів до акумуляції призводить до накопичення їх у рослинних і тваринних організмах через підвищення біодоступності, подолання біобар'єрів, зв'язування з нуклеїновими кислотами та білками.

У статті досліджено особливості накопичення наночастинок металів у рослинах, вплив на проростання і вегетацію, обмінні процеси та врожайність. Проаналізовані відомості щодо застосування наночастинок металів у тваринництві як альтернативи кормовим антибіотикам задля підвищення продуктивності. Встановлено, що рідкоземельні елементи можуть активізувати обмін білків та інших поживних речовин шляхом стимулювання діяльності гормонів, індукування синтезу металотіонеїнів та зростання коефіцієнту конверсії корму. Встановлені зміни прооксидантно-оксидантного статусу крові тварин за використання препаратів з наночастинками діоксиду церію та зміни показників гомеостазу. Застосування рідкоземельних елементів є позитивним для домашньої птиці через інтенсифікацію виробництва яєць, їх ваги та заплідненості інкубаційних яєць. Встановлений вплив наночастинок металів на окисно-відновний потенціал та процеси пероксидного окиснення ліпідів в організмі тварин. Аргументовано використання нанодисперсного діоксиду церію як перспективного нанобіоматеріалу для біологічного та медичного застосування та необхідність подальших досліджень задля вивчення всіх можливих механізмів його біологічної активності.

Ключові слова: НАНОЧАСТИНКИ, ДІОКСИД ЦЕРІЮ, БІОТРАНСФОРМАЦІЯ, ПРОДУКТИВНІСТЬ, ОКИСНО-ВІДНОВНІ ПРОЦЕСИ

ПЕРСПЕКТИВЫ ИСПОЛЬЗОВАНИЯ НАНОЧАСТИЦ ЦЕРИЯ В СЕЛЬСКОМ ХОЗЯЙСТВЕ

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В последнее время нанотехнологии завоевывают ключевые позиции в разных сферах знаний благодаря особенному положению наночастиц по размеру и физико-химическим свойствам. Высокая способность наночастиц металлов к аккумулированию приводит к накоплению их в организмах растений и животных из-за повышения биодоступности, преодоления биобарьеров, связывания с нуклеиновыми кислотами и белками.

В статье исследовано особенности накопления наночастиц металлов в растениях, влияние на прорастание и вегетацию, обменные процессы и урожайность. Проанализированы сведения о применении наночастиц металлов в животноводстве в качестве альтернативы кормовым антибиотикам для повышения продуктивности. Установлено, что редкоземельные элементы могут активизировать обмен белков и других питательных веществ путем стимулирования деятельности гормонов, индуцирования синтеза металлотионеинов и роста коэффициента конверсии корма. Установлены изменения прооксидантно-оксидантного статуса крови животных при использовании препаратов с наночастицами диоксида церия и изменения показателей гомеостаза. Применение редкоземельных элементов является положительным для домашней птицы через интенсификацию производства яиц, их веса и оплодотворяемости инкубационных яиц. Установлено влияние наночастиц металлов на окислительно-восстановительный потенциал и процессы перекисного окисления липидов в организме животных. Аргументировано использование нанодисперсного диоксида церия как перспективный нанобиоматериал для биологического и медицинского применения и необходимость дальнейших исследований для изучения всех возможных механизмов его биологической активности.

Ключевые слова: НАНОЧАСТИЦЫ, ДИОКСИД ЦЕРИЯ, БИОТРАНСФОРМАЦИЯ, ПРОДУКТИВНОСТЬ, ОКИСЛИТЕЛЬНО-ВОССТАНОВИТЕЛЬНЫЕ ПРОЦЕССЫ

The current stage of science development is characterized by comprehensive miniaturization of technological processes that contribute to a fundamentally new direction — nanotechnology. In recent years, nanotechnology wins leading positions in chemistry, biology, medicine and agriculture [10, 28, 47, 66]. Nanoparticles are intermediate between individual atoms and molecules; they are characterized by fundamentally different physical and chemical properties in comparison with the macrocosm [10, 55, 73].

The high adsorption activity of nanoparticles caused by increasing of their specific surface area, result in the ability to absorb per mass unit much more substances than macroscopic dispersion [30, 77]. A large surface area increases the absorption capacity and the possibility for adsorption on nanoparticles various contaminative with easier transport into cells [28, 30, 66]. Ultra small sizes of metal nanoparticles cause increasing of bioavailability, overcoming the biological barriers (blood-brain barrier, blood-tissue interface, and placental barrier), and ability to formation of chemical bonds with nucleic acids and proteins, embedding into cell membranes, penetration to organelles with changing their functions. High penetrating capability of metal nanoparticles leads to their accumulation in plant and animal organisms as well as microorganisms transferring them on the food chain, and as a result increasing revenues to the human body [1, 7, 10, 11, 55].

Due to the small size, nanoparticles easily penetrate into body through the respiratory system, digestive system, skin and show more obvious biological activity due to the large surface area per unit mass [10, 16, 35, 61]. Changing of the physical and chemical mechanisms of nanoparticles caused to the fact that most of the atoms are located on the surface. This arrangement changes the physical, chemical, biological and toxicological properties of substances and promotes the interaction of nanoparticles with an alive organism [28, 47, 66].

Target organs and formation of the response reaction mechanisms vary for different metal nanoparticles. They are able to induce reactive oxygen species, to disrupt membrane structures, to penetrate through the tissue barriers, to flow into the cells and interact with intracellular components [7, 28, 66]. Survey questions of positive effect and toxicity of metal nanoparticles are ambiguous and multifaceted requiring an integrated approach. It is particularly concerns nanoparticles used in pharmacology, medicine and agriculture, which promotes to their direct entering the human body [7, 28, 47, 63, 66, 81].

To the list of ten priority nanomaterials created by experts of the Inter-Organization Programme for the Sound Management of Chemicals (IOMC) and the Organization for Economic Co-operation and Development (OECD) include cerium dioxide nanoparticles [7, 66].

Cerium dioxide nanoparticle is a promising material widely used in modern high-tech industries [19, 38, 73]. The significant interest shown in recent years to the cerium investigation is primarily due to the fact that the transition of the compound in nanocrystalline state significantly changes its physical and chemical properties, and the nature of these changes is very unusual [67, 73]. In particular, unlike a number of substances (for example, common gold), the unit cell parameter CeO_2 increases with decreasing particle size. At the same time, there is a change of oxygen non-stoichiometry cerium dioxide due to increase in the proportion of atoms on the surface of the particles that causes changes in its electronic and electrical properties [11, 28, 66, 67].

Clearly marked effect of particle size on the physicochemical properties of cerium dioxide causes nanodispersed unique biological activity of the material. Prospects and features of its application are determined by two main factors: low toxicity and high level of oxygen non-stoichiometry. The first factor provides comparative safety of cerium dioxide nanoparticles use *in vivo* [49]. The second factor causes activity of nanodispersed CeO_2 in redox processes in living cells, especially in the case inactivation of reactive oxygen types [7, 28, 66]. Specific properties of CeO_2 include the ability to regenerate oxygen non-stoichiometry, which is expressed in the ability of nanoparticle ceria return to original state after participating in redox processes in a relatively short period providing the ability their repeated use [28, 66, 68].

Currently, a large number of plant products is grown with the use of nanotechnology. It is expected that in the near future over 15 % of all products at the world market will certainly include nanotechnology in their production process [37]. Designed nanoparticles (1 to 100 nm) may possess different physical and chemical properties than those found in nature; and their impact on human health must be evaluated based on their size and shape [27, 49, 62, 88].

Plants are capable to significant metals accumulation that can significantly (hundreds times exceed physiological concentrations [29, 43]. It is believed that this provides some protection of plants from insects and herbivores. The use of nanoparticles for plant growth and plant diseases treatment was referred previously [9, 27, 52, 65, 69, 94]. Nanomaterials may be applied for the diagnosis of some plants diseases using labeled nanoparticles [43, 78]. It may be helpful to increase the production of many dwarfish edible plants, such as spinach, radishes and some grains, for example, corn, rice and wheat [58].

Nanotechnology can be used for controlled release of drugs, pesticides, agrochemicals, for effective use of minerals without disrupting the livelihoods of beneficial insects [9, 44, 45, 48]. It provides conversion of organic waste into marketable products [5, 48, 88]. Nanoparticles may show entirely new or improved properties compared with larger particles of particulate material from which they are made [70]. Biodegradable organic waste of plants can be used for nanoparticles synthesis, because of the content phenols, flavonoids and reducing agent [17, 36, 50, 60]. The current strategy of producing nanoparticles, particularly cerium dioxide, involves the use of principles and approaches of “green chemistry” (green synthesis) [27].

Since the absorption of minerals by the plant is a non-selective, some metal ions in combination with anions can cause the toxicity if they exceed the permissible limits. When absorbed, the nanoparticles can accumulate by various parts of the plants and form complexes with a carrier proteins. It have established that different plant species selectively accumulate individual nanoparticles. If the size of the particles is larger than root pores, they are accumulated on the surface, and when they are smaller, they are absorbed and transported to other parts of the plant. The conditions of absorption and biological distribution of cerium oxide nanoparticles in a many crops, including wheat [62], pumpkin [62], sunflower [62], beans [3, 41], cucumbers [37, 39, 91], radish [75, 90], tomatoes [37], maize [37, 92], lucerne [15, 37], buckwheat [15] and rice [57] in native have been investigated. Mainly, Cerium oxide nanoparticles have a greater adsorbing ability in plant roots than in other plant tissues (such as leaves or twigs) [41, 62, 90]. The absorption and distribution of nanoparticles depend on several factors, including size [62, 90, 91], concentration [37, 41, 91], agglomerations [91], and ways of input [76] and the ability to transforming, for example, to form such insoluble compounds Ce as $CePO_4$ [62].

Researches for the action of nanoparticles of cerium dioxide on the seed germination and root elongation, and leaf crop growth were conducted [76]. In the case of cutting or putting into the soil nanoparticles penetrate and transported to various parts of the plant. Some nanoparticles remain in the extracellular matrix; others remain inside the cells [20, 41].

Dosage and absorption of nanoparticles can vary. Nanomaterials can be administered by spraying or by mixing with soil. Experiment with nano-CeO_2 on soy and buckwheat showed an increase in yield and quality of crops [15, 54]. However, in other studies [46, 57] in the case of CeO_2 soybean processing reduced number of formed leaves has been found. Short-stem plants can be grown using nanoparticles of CeO_2, but none increase in yield were found. This demonstrates once again the importance of physical and chemical properties of nanoparticles — a method for producing, size, zeta potential values, biocompatibility of nanoparticles shell [28, 47, 55, 67].

The nanoparticles influence the biological object on the cellular level increasing the efficiency of plants metabolism, and also participate in shaping the balance of trace element, so they are bioactive. They are digested slowly; but their ionic forms are easily incorporated into the biochemical reactions [45, 49]. So, a prolonged effect of plants nutrition from huge specific surface area (hundreds of square meters per 1 gram of substance) is achieved. Preparations are made in small doses and do not pollute the environment.

Nanoparticles take part in the processes of electron transfer, enhance the action of enzymes, convert nitrates into ammonia nitrogen, intensify cellular respiration, photosynthesis, synthesis of enzymes and amino acids, carbohydrate and nitrogen metabolism, and therefore can directly affect the mineral nutrition of plants [20, 26, 27, 38, 49, 78]. Having high mobility, they interact with each other and conglomerate on the surface of the plants adjusting target effects [44, 45]. This causes stimulating plant growth to raise the yield by 25–50 [8].

Despite the risks, nanotechnologies are widely implemented in all areas of technologies, material study and agriculture. The impact of nanoparticles on the environment and human health are subjected to intense debate [4, 45, 49, 58].

Now metabolism of cerium nanoparticles in plants is intensively studied by the scientific community. It is necessary to consider not only the uptake and localization of particles in plants but impact on the functions of ecosystems, biodiversity and productivity of crops also [5, 20, 38, 53, 89, 93]. Getting in a biological system, nanoparticles face a number of physical and chemical characteristics of the organism that affect their properties and can change the answer [62, 78]. These features are largely due to the ability to undergo redox cycle between two natural oxidation states (Ce^{3+} and Ce^{4+}) [9]. However, previously believed that nanoparticles of CeO_2 were stable [77] and low soluble [13, 59] or insoluble [40, 57] under surrounded conditions, depending on the carrier substances, pH and particle size [61]. Dissolution of nanoparticles depends on the ratio between Ce^{3+} and Se^{4+} on the surface layer [62]. With decreasing size the nanoparticles free from oxygen vacancies in the lattice, more and more what results in reducing the number of local Se^{4+} [30].

It was revealed that CeO_2 nanoparticles toxicity for *E. coli* depends on surface of nanoparticles and varies according to the presence of the bacteria [74]. Adding phosphate to the nanoparticles can stop this redox cycle by capturing Se^{3+} in $CePO_4$ [68].

The inclusion of nanoparticles in plant cells demands they pass through the cell wall, which has a pore size in most species by the maximum 5 nm [44], while the transition from the roots through the intercellular space is blocked by Casparian strip of the endoderm root. Despite these obstacles, it was reported that nanoparticles larger than 5 nm can be moved from the roots into the shoots of some plants depending on their concentration [58]. It was also shown that nanoparticles of CeO_2 could bypass Casparian strip in young tissues [42]. The accumulation of Ce nanoparticles depends on the plant species. Applying it for sunflowers results in accumulation in leaves, while there were no significant changes after using Ce nanoparticles for pumpkins and wheat. If the particles were larger than 20 nm, Ce translocation from roots to shoots did not occur [62].

Currently there are very few studies concerning possible changes of CeO_2 nanoparticles in plants. There are reports, that rhizosphere of cucumber transforms CeO_2 nanoparticles to the $CePO_4$, and 21.5 % of available in the leaves Cerium was converted into carboxylate form [17]. 21 % CeO_2 nanoparticles were found in soybean nodules in converted forms, however biotransformormed CeO_2 in soybean pods were not found [25].

Nanoparticles of cerium are able to biotransform in the roots of plants to cerium phosphate [92]. On the other hand, the possibility of transformation of CeO_2 in the roots of cucumber, alfalfa, tomato and corn is denied [37, 92].

Recent years, the literature contains reports on the use of nanoparticles of metals, including cerium in animal husbandry, because the use of antibiotics as growth promoters prohibited in the EU since 2006 [32]. Therefore, scientists and livestock producers began an intensive search for alternatives to feed antibiotics. Essential oils, pre- and probiotics, organic acids and enzymes currently successfully used instead of antibiotic feed additives. A number of rare earth elements (REE), including cerium, can be successfully used as a new natural supplement to the feed for improve animal productivity [2, 6, 17, 18, 22, 23, 24, 86, 87].

There are reports that REE can activate proteins and other nutrients metabolism by stimulation of hormones activities in particular growth hormone and T3 [2, 7, 87], induce the synthesis of metallothioneins and increase the content of glutathione in the liver [31]. In addition, antimicrobial and antioxidant action REE for animals was established [19, 22, 83]. In case of their use in the diet of pigs (100 mg/kg), a positive effect on feed conversion rate [80] and growth rates was achieved [12, 22, 51, 80].

The changes blood prooxidant-oxidant status of cows with hypogonadism after treatment with kaplaestrol drug containing nanoparticles SeO_2 (cerium dioxide) were determined [63]. The efficiency of the repair and restoring of ovarian reproductive ability of cows were determined. The investigation of changes in the homeostasis morphological and functional state of the mammary gland of cows in dry period in case of deficits of carotene, vitamin A, failures in the prooxidant-antioxidant system and with the use of drugs kaplaestrol + CeO_2 + prozon and ovaks-1 + prozon was done. The use of nanoparticles of cerium in combination with drugs helps to normalize the structure and function of the mammary gland, and increase the level of maternal immunoglobulin's [34].

The application of REE had positive results for poultry [6, 12, 18, 21, 82, 83, 84]. In these studies, the addition of different levels of rare earth elements (200, 400, 600 and 800 mg/kg) promoted a significant increase in egg production, egg weight and hatching eggs fertilization rate of 6-month-old laying hens [82]. It was found that the addition of different levels of REE-nitrate to diet of laying hens (300, 400 and 500 mg/kg) significantly improved the rate of egg formation and their weights [87].

Dietary REE citrate improves broilers productivity [23]. One of the mechanisms of influence is the increased secretion of digestive system [51], in particular, the secretion of hydrochloric acid in the stomach [85]. Adding rare earth elements to the diet promoted a significant increase of superoxide dismutase activity in the blood of fish [79] and chickens [83].

Adding of different amounts of cerium oxide for laying hens (0, 100, 200, 300 or 400 mg/kg) had no significant effect on feed intake and egg weight, though improves feed conversion and increases ($P<0.05$) egg production. Eggs quality criteria, except tensile strength of the shell, were not changed. In particular, the addition of 200 and 300 mg/kg of cerium oxide to feed of hens resulted in significant ($P<0.01$) increase of eggshell strength at break. The concentration of calcium and phosphorus in the blood serum increased significantly ($P<0.05$) due to the adding of 100 mg/kg of cerium oxide. It was also noted that serum superoxide dismutase (SOD) and the concentration of malondialdehyde (MDA) significantly decreased after adding cerium oxide. Different doses of cerium oxide had no significant effect on the activity of aminotransferase, glucose, glycerol, total cholesterol, HDL and LDL in the serum. In the case of inclusion cerium oxide to the diet of laying hens a significant reduction of TBARS in egg yolks was observed [6]. At the same time, additions of cerium oxide improves oxidation stability of eggs, what may have a beneficial effect on storage time [21]. In the applicable dose, nanocrystalline ceria does not accumulate in eggs and parenchymal organs of birds [63].

Rare-earth elements have similar characteristics to Ca [24, 26], which can lead to increased strength of eggs shell. It is believed that cerium oxide can also increase the calcium content in serum. Therefore, the concentration of calcium in the blood serum of Japanese quail fed low concentrations of REE (50 and 100 mg/kg) increased significantly [95]. Other studies [23] report that supplementation of chickens diet with REE do not affect the concentration of calcium in serum. With increasing of REE content in the diet of broilers glucose concentration in the blood decreases [2]. The content of calcium and phosphorus in the blood serum were increased by low concentrations of cerium oxide supplementation (100 mg/kg), but the high concentration of cerium oxide has no influence.

Watering of quails with nanocrystalline cerium dioxide positively affects egg productivity. Using of nanotseria at 1 mM/liter of drinking water increased egg quail quantity by 7.8 %, weight eggs by 16.9 %, the intensity of egg production by 6.7 %. Drinking nanotseria at doses of 0.1–10 mM/L does not cause accumulation in eggs and parenchymal organs [71]. The influence of nanotseria on the rate of growth and feed intake of young quail were found [72].

The effect of nanocrystalline cerium dioxide is studied and lethal and semi lethal doses are determined. Ld_{50} for nanocrystalline cerium dioxide is more than 2000 mg/kg, which confirms the identity of the compound to class V toxicity and indicates a very low toxicity [64].

The positive antibacterial potential of nanoparticles CeO_2 against poultry pathogens such as *Klebsiella sp.*, *E. coli*, *Staphylococcus sp.* and *Salmonella sp.* were shown [56, 74].

The high degree of biocompatibility, low toxicity and catalytic activity of nanodispersed cerium dioxide allow considering it as a promising nanobiomaterial for the use in biology, medicine and agriculture. Nowadays all possible mechanisms of its biological activity are poorly studied and need further research.

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