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Targeting Cancers: Uncovering the Potential Roles of Potato Tissue Culture as Anti-Cancer Agents

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Abstract: Plant tissue culture is a technique that enhances the quality and quantity of potatoes. Potatoes are a significant crop and are primarily used in the world. It is a staple food in many countries, where millions of tonnes are produced annually. It is an essential source of many nutrients, such as proteins, carbohydrates, vitamins, and beta-carotene. In addition, potatoes are being used as therapeutic agents against cancer and other human diseases as well. Potatoes are on the third list after wheat and rice. To overcome food shortages and malnutrition, there are two methods used for producing potatoes: the first is sexual, which is seed propagation, and the second is asexual, which is plant tissue culture propagation. Conventional potato breeding is a uniform method, but it is unsafe because there is a risk of pathogen attack. In a laboratory setting, the tissue culture of potatoes produced millions of plants with nutrient-rich medium under controlled environmental conditions that prevent pest attacks. Some environmental stresses, such as salinity and water scarcity, affect potato yield and production; however, applying nanoparticles like organic, inorganic, and silicon dioxide enhances potato quality and combats stress. Biotechnology has proven to be helpful in addressing all these issues. This review discusses the significance of potatoes, their production through the tissue culture technique, and the application of nanoparticles to improve the growth, and impact of potatoes on human health.

Keywords: Cancer; Nanoparticle; Potato; Tissue culture

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1. Introduction

The potato is a very important Dicotyledonous plant and is an important member of the Solanaceae family. There are almost 2000 species of this plant in the world [1]. The potato shows much exceptional genetic variety among cultivated plants. This variety strengthens its position as a key staple crop [2]. Historically, potatoes were grown commercially in cool climates with long daylight periods; this was due to their value as a food source. They are an important source of starch, proteins, vitamins, minerals, and trace elements and provide a significant amount of essential nutrients in a dry, concentrated form [1]. Potato is grown in almost 150 countries all around the world and consumed by over one billion people of the world as food and most of them live in poor countries because they give exceptionally high yield and energy [3,4]. Beyond food, potatoes have many industrial uses, from processed products to biofuels, and are used as raw materials for the production of different industrial products [5].

There are two main methods for multiplying potato plants: sexual reproduction using botanical seeds (true potato seeds) and asexual reproduction using vegetative parts of the plants, primarily tubers [6]. Traditionally, seed potatoes, which are tubers specifically chosen for propagation, have been the preferred approach for growing new potato plants. Conventional breeding of potatoes has many drawbacks. It results in a low multiplication rate, and there is a risk of disease and pathogen attack [7,8].

In recent years, tissue culture techniques have emerged as a promising alternative for vegetatively propagating potatoes [9]. This new technology involves growing plant cells or tissues in a controlled, sterile environment. Tissue culture offers a significant advantage over traditional potato propagation. Plant tissue culture and vegetative propagation are becoming increasingly popular for multiplying potato plants in both rich and developing countries [10]. This is not just about getting more potatoes quicker; it also allows scientists to improve the potatoes themselves and protect existing potato varieties [11]. Instead of relying on traditional methods where one potato might only produce a handful of new ones, tissue culture can create thousands of new, identical potato plants in a much shorter time. By starting with tiny plant bits under controlled conditions, scientists can avoid spreading diseases that might be present in whole potatoes used for planting [12].

2. Plant tissue culture media

Several media formulations are used for the majority of all cell and tissue culture work. The media formulations include those described by White, Murashige and Skoog (MS Media) [13], Schenk and Hildebrandt, Nitsch, and Lloyd and McCown mediums are all high in macronutrients while the other media formulations contain considerably less of the macronutrients. Plant tissue and cell culture media are generally made up of some or all of the following components: macronutrients, micronutrients, vitamins, amino acids or other nitrogen supplements, Sugar, Undefined organic supplements, solidifying agents or support systems, and growth regulators [13]. **Table 1** shows MS medium preparation for plant tissue culturing.

Table 1. MS medium preparation for plant tissue culturing

Chemicals	Concentration
MS media	4.43 gm per liter
Sucrose	30 gm per liter
IAA	1 mg per liter
KH_2PO_4	100 mg per liter
Vitamins	10 ml per liter
BAP	8 mg per liter
Gellan gum	2.2 gm per liter

3. *In vitro* micropropagation of potato

Tissue culture is the regeneration of new plants from disease-free parts. Over the past 50 years, the application of the tissue culture technique has been more conspicuous in potatoes than in any other crop [14]. To grow healthy potato plants in a lab using tissue culture, it is crucial to keep everything super clean and free of germs. This means sterilizing all the tools, containers, and the unique nutrient mix (media) used to feed the tiny plant parts. Even the air and the workplace need to be kept germ-free [15]. To achieve this, scientists work in extraordinary cabinets with clean airflow. For growing potato plants in a lab, a particular nutrient mix called MS media has been very successful in many experiments [16]. However, before putting any potato plant bits (explant) into this mix, the most crucial step is to sterilize them thoroughly. Different disinfectants can be used, such as bleach (sodium hypochlorite) or alcohol (ethanol), to kill any germs on the surface of plant bits. In this case, they were dipped in a mild bleach powder for a short time, followed by washes with a disinfectant and an alcohol. Finally, they were rinsed many times with clean water to remove any leftover traces [7]. By using special enzymes to remove the cell wall, the inner part of a potato cell, such as the protoplast, can used to grow a complete plant. Different enzyme mixtures, such as cellulase and macerozyme, are used to see which ones worked best for isolating potato leaf protoplasts. The potato protoplast is purified and immersed in petri dishes. The protoplast grows to a complete plant [17-19]. There are seven steps used in the tissue culturing of potatoes which include

3.1. Suckers isolation

For *in vitro* propagation of potatoes, we use suckers as ex-plant [20]. Suckers were first collected from the glasshouse utilizing cutting the stem and tearing apart roots so that suckers could be isolated and removed from the leaves and upper scale of the plant through a knife and cutter. Further suckers were dipped in 30 % of Clorox solution for 30 minutes [21]. Then suckers were further washed with 50 % of Clorox in a laminar flow hood for initiation and culturing [22].

Figure 1. Suckers isolation from the field

3.2. Meristem excision

The suckers obtained were then cultured in MS media. All the processes were carried out in the biosafety cabinet [23]. The suckers were cultured and kept in a growth room for about one month. The media is constituted of different ingredients by different volume concentrations. The pH was maintained up to 5.7 to 5.8 [24].

Figure 2. Meristem excision and *in vitro* meristem culturing

3.3. Shoot regeneration

After one month of sucker culturing, the cultures were then transferred into multiplication media for organogenesis in order to get shoots and leaves. The process is carried out in a biosafety cabinet and allows the regeneration of more virus-free plants from a single callus, followed by maintaining the pH up to 5.7 to 5.8 [24]. The shooting media preparation recipe is shown in **Table 2** and shoot culturing under sterile conditions is displayed in **Figure 3**.

Table 2. Shooting media preparation recipe

Chemicals	Concentration
MS media	4.43 gm per liter
Sucrose	30 gm per liter
IAA	1 mg per liter
KH_2PO_4	100 mg per liter
BAP	3 mg per liter
Vitamins	10 ml per liter
Gellan gum	2.2 gm per liter

Figure 3. Shoot culturing under sterile conditions

3.4. Root regeneration

After 4–5 subculturing of shoot regeneration and development of shoots and leaves from callus, it was further cultured in another media known as rooting media [25], which led to the development of roots of plants; all process was carried out in a biosafety cabinet and allowed to regenerate the roots. The pH of the media was maintained between 5.7 and 5.8 [24]. The rooting media recipe is presented in **Table 3**, while **Table 4** shows the number of shoots/cultures produced during each subculture.

Table 3. Rooting media recipe

Chemicals	Concentrations
MS media	4.43 grams per liter
Sucrose	30 gram per liter
IAA	2mg per liter
KH_2PO_4	I00 mg per liter
Vitamins	10 ml per liter
Gellan gum	2.2 gram per liter

Table 4. Number of shoots/cultures produced during each subculture

Ex-plant number	1st sub-culturing	2nd sub-culturing	3rd sub-culturing	4th sub-culturing
1	1	4	12	35
2	1	3	12	36
3	1	1	4	12
4	1	2	6	18
5	1	2	7	12

3.5. Hardening

After 1.5 to 2 months, the development of the complete plant, including roots, shoots, and leaves, the plant is then further carried to the process of hardening so that the plant be acclimatized to the environment [26] before it gets transferred to the field as the plant develops through tissue culture are so fragile to avoid any type of stresses; this includes the carrying out plant in shopping bags filled out with pet mass in glasshouse avoiding the major stresses including both biotic and abiotic stresses (**Figure 4**) [27].

Figure 4. Hardening under a controlled environment and in the glasshouse

3.6. Field transplantation

When plants survive in the glasshouse and withstand stresses, they are further carried out from the glasshouse and transferred to the field, and the plant is ready to start a new cycle [28]. **Figure 5** shows the potato culturing flow sheet diagram.

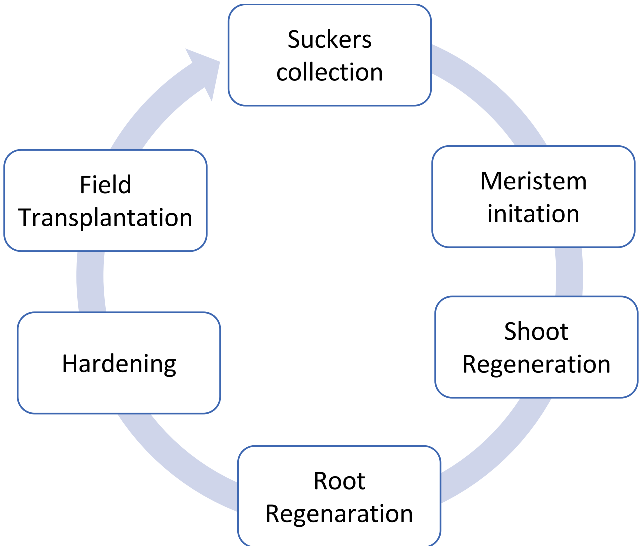

Figure 5. Potato culturing flow sheet diagram

4. The issues in the cultivation of potato

Potato is an essential food for any country, but it can face various viruses, fungi, and bacterial attacks [29]. The total loss caused by these diseases is 30–100%. Viruses are the leading cause of disease [30]. To overcome it, both biotechnological and conventional techniques are applied. Meristem culture using the plant tissue culture technique is introduced because the first virus-free potatoes were produced using meristem, and the reason is that viruses are unable to invade the meristem tissues [31]. These tissues remain in the active dividing phase throughout the vegetative phase of the plant. The larger the size of the meristem tissue, the more remarkable the size of the generated plant [12,32,33]. Potato cultivation faces different climate changes, which increase temperature, salinity, and scarcity [34-36].

As the world's population has boomed in recent decades, so too has the demand for food [37]. This has put a significant strain on our available land, pushing us to convert more and more areas into farmland to keep up with the need to grow crops [38]. However, a significant threat to this increased food production is the need for more water. Water scarcity is a severe issue affecting plant growth and overall agricultural output around the globe [39]. This problem is only to worsen due to climate change, which is likely to lead to a rise in the rate at which water evaporates from the earth's surface [40]. By 2050, experts predict that as much as half of the world's currently usable farmland could face severe problems due to water stress. This lack of water has a profound impact on plants, affecting a wide range of complex processes within them, both physically and chemically. When plants are deprived of water, their outward appearance suffers. Leaves become smaller, and their overall growth is stunted. The roots, which are responsible for taking in water and nutrients from the soil, struggle to function correctly in dry conditions [41]. This disrupts the plant's ability to regulate its internal balance of water and essential minerals, hindering the movement of these nutrients to the rest of the plant [42].

Furthermore, water stress creates a condition within plants similar to what we might experience as stress [43]. This triggers a chain reaction where the plants produce harmful molecules called reactive oxygen species.

These molecules, along with the lack of water, damage the delicate membranes surrounding the plant's cells. As a result, the plant's overall health and ability to function are compromised [34]. There is a big problem with not having water to grow food around the world, especially in hot and dry areas. Not enough water hurts most crops, and potatoes are especially feeling the pinch. All stages of potato growth suffer when water is scarce, but the times when potatoes are forming and growing their tubers are the most critical [11]. This lack of water can hurt the rate at which they make food, their ability to take in air, and how much water they release. It can also affect the green pigment in their leaves [44,45].

5. Abiotic environmental stress

One of the most important and harmful abiotic environmental stresses is salinity. Salinity means there is enough salt in the soil and water that plants are taking in through their roots [46]. It is common in dry areas all over the world and hinders plant growth and overall production. A staggering 6% of the world's land, translating to over 800 million hectares, suffers from salinity [47]. This saltiness severely hinders plant growth, forcing plants to adapt and develop various survival strategies [48]. The problem lies in the excess of salt ions within the soil or water. This disrupts plants on a fundamental level, affecting their physical form, internal processes, and chemical makeup [49]. In a salty environment, plants absorb an unhealthy amount of sodium ions at the expense of vital nutrients like potassium and calcium [50]. As sodium levels increase in leaves, stems, and other parts with rising salinity, a nutritional imbalance occurs. This imbalance directly translates to stunted plant growth and a decrease in material. Salt stress also creates a condition within the plants known as osmotic stress. This made it harder for plants to take in water, leading to a reduction in the rate at which they produce food [51]. Additionally, pigments responsible for photosynthesis break down, further hindering food production. Salt stress also disrupts the delicate balance of water absorption and nutrient uptake by plants [52]. More salt and water in the soil is not suitable for potatoes. It stunts their growth, reduces their size, and uses water efficiently [53,54]. Potato production is affected by different abiotic stresses, and it is essential to overcome them [55-57].

6. Application of nanoparticles for crop improvement

A technology called nanotechnology is introduced, and different nanoparticles are applied to plants for crop improvement from environmental stresses [58]. These particles benefit plants in several ways as they affect the plant's metabolic pathways. Some scientists are also using nanoparticles to stimulate the production of plant hormones that regulate and stimulate plant growth and metabolism when plants are facing stress conditions [59]. Studies have also shown that treating soil with these nanoparticles protects the root system and promotes growth even under stress [60]. Nanoparticles include organic and inorganic particles, and they are used all over the world. They have applications in agriculture and plant biotechnology [61]. Their applications in agriculture have increased in recent years, and they are different from large-sized particles in both physical and chemical properties [62]. They have many advantages and can speed up plant germination; they can help plants bear different biotic and abiotic stresses such as salinity, temperature, and water scarcity. Various kinds of nanoparticles are used to help potato plants recover from stress conditions, but silicon dioxide is widely used to handle salinity and water scarcity [45]. Silicon dioxide nanoparticles provide greater surface area and high surface reactivity. Silicon nanoparticles can increase plant growth and defend against disease and pests [63]. The use of silicon causes increased fruit weight. Studies have shown that this technology improves production from plants and nanoparticles because these particles of silicon dioxide are used as exogenous material and improve plant physiology and morphology [44,64,65].

7. Application of silicon dioxide nanoparticle

As silicon nanoparticles (NPs) are small and are mostly 20 nm, they can be applied to plants in different ways [66]. The powdered NPs are mixed with a liquid nutrient medium and applied to plant roots, where roots absorb nanoparticles. Second is the direct supplement of silicon nanoparticles to the soil, and it depends upon the soil [66]. The foliar method is used in which silicon dioxide nanoparticles are sprayed on plants' leaves and then absorbed by leaves' stomata. Direct application of silicon nanoparticles to plants by soil is more effective than the foliar method [67]. Silicon is the second most abundant mineral in soil, and it reduces the negative effect of NaCl in potatoes and declines its absorption by roots. It activates different enzymes in plants and produces auxin. foliar applications increase plant height [52]. Water deficit closes potato stomata, and gas exchange is stopped, but the application of silicon nanoparticles maintains stomata structure and recovers them to perform their normal activity compared to untreated potato plants. In this way, stomata exchange gases and photosynthesis occur, and the negative effects of water deficit and ion exchange also occur [44].

8. Impact on human health

Population-based epidemiological studies have highlighted the role that nutrition plays a vital role in preventing metabolic illnesses, including diabetes, cancer, and cardiovascular diseases, which are linked to food and are on the rise globally [68]. Research repeatedly highlights the consumption of fruits and vegetables as preventive benefits against certain types of chronic illnesses. Potatoes have not received the same appreciation as other vegetables due to the controversy surrounding them [69], including claims that they may contribute to the development of diabetes and obesity. Potatoes, conversely, contain comparatively large amounts of essential phytonutrients with demonstrated bioactivities that may prevent the onset of chronic diseases [70]. In human cell culture, experimental animal investigations, and human clinical trials, potatoes have demonstrated encouraging health-promoting benefits, including anti-cancer, anti-hypercholesterolemia, anti-inflammatory, anti-obesity, and anti-diabetic qualities. Phenolics, anthocyanins, fiber, and starch, along with other nutritionally significant components like lectins [71], glycoalkaloids, and proteinase inhibitors, are believed to contribute to the health advantages of potatoes. Depending on the situation, many biological activities have been attributed to the compounds found in potatoes [72], some of which may be advantageous or detrimental. Therefore, long-term studies that control for fat intake and examine the relationship between potato consumption and diabetes, obesity, cardiovascular disease, and cancer are required [73].

8.1. Anticancer effects

Studies on the anti-tumor effect have shown that applying potato extracts to cancer cells inhibits their proliferation [74]. Researchers have linked antioxidants in potatoes, such as fiber, proteinase inhibitors, glycoalkaloids, phenolic acids, and anthocyanins, to cancer cell growth inhibition *in vivo* and *in vitro* [70]. Commercially available potato fiber extract (Potex) has demonstrated antiproliferative effects in various tumor cell cultures [75]. The fiber extract altered tumor cell morphology, reducing cancer cell motility and triggering apoptosis. Potatoes with colored flesh are a great source of anthocyanin, with several health advantages [76]. Several studies have shown that purple-fleshed potatoes inhibit colon cancer cell growth and increase apoptosis rates compared to those with white or yellow flesh.

Anthocyanin reduces stomach cancer due to benzopyrene. The anthocyanin fraction from genotype CO112F2-2 and extracts from four speciality potatoes effectively inhibited the growth of both androgen-dependent (LNCaP) and androgen-independent (PC-3) prostate cancer cell lines [77]. They did this by increasing the levels of the cyclin-dependent kinase inhibitor p27 [78]. The anthocyanin-containing potato extract released the proapoptotic Endo G and AIF proteins from mitochondria and took them up by the nucleus [79]. Extracts from the *Solanum jamesii* tuber have been shown to kill and stop the growth of human colon cancer cells (HT-29) and human prostate cancer cells (LNCaP). The red Mountain Rose cultivar, high in anthocyanins and chromogenic acid derivatives, stopped breast cancer more effectively in rats chemically induced to get it than the white Russet Burbank cultivar [80].

Potato polyphenols are beneficial against human liver, colon, and prostate cancer cells. Research using single phenolics revealed that chromogenic acid might be the main component potentially responsible for the antiproliferative effect [81]. Chromogenic acid stopped the growth of A549 human lung cancer cells in the JB6 mouse epidermal cell line. It also stopped the activation of AP-1 and NF-kB by UVB or TPA, inflammatory mediators linked to cancer. In addition, chromogenic acid considerably slowed the growth of colon and liver cancer cells in a lab setting [82]. Several studies have shown that potato glycoalkaloids stop the development of human cancer cell lines, including those from the stomach (HT29), liver (HepG2), colon (HT29), cervix (HeLa), and lymphoma (U937) [83].

It was discovered that *α*-chaconine was more effective than *α*-solanine. *α*-Chaconine induced apoptosis in HT-29 human colon cancer cells by activating caspase-3 and inhibiting ERK 1/2 phosphorylation, and it reduced lung cancer metastasis *in vitro* by suppressing the phosphoinositide 3-kinase (PI3K)/Akt/NF-kB signaling pathway and that LNCaP and PC3 prostate cancer cells died more quickly and were less likely to survive when they were exposed to β-chaconine and gallic acid found in potato extracts [84]. However, a recent investigation revealed that potato glycoalkaloids had little apoptotic activity and a cytotoxic impact comparable to other cancer medications. Moreover, studies have documented the anti-cancer properties of additional substances such as potato lectin and potato protease inhibitors 1 and 2 [85].

8.2. Role in antioxidant and anti-carcinogenic

The function of potato antioxidants includes the anti-carcinogenic properties of phenolic acids and anthocyanins [86]. Anthocyanins found in steamed purple and red potatoes inhibited the growth of benzopyrene-induced stomach cancer in mice. Potato extract anthocyanin fractions activated both caspase-dependent and caspase-independent pathways, which in turn caused cytotoxicity in prostate cancer cells. Compared to white and yellow flesh potatoes, purple flesh potatoes with a high anthocyanin content inhibited colon cancer cell growth and increased apoptosis. A recent study found that purple-fleshed potato extract eliminates colon cancer stem cells, suppressing colon carcinogenesis [87]. Chlorogenic acid, the primary phenolic acid in potatoes, effectively combats human liver, colon, and prostate cancer cells. It also significantly slows down colon cancer and prostate cancer cell growth [88].

8.3. Glycoalkaloids

The primary steroidal glycoalkaloids found in potatoes, α-solanine, and α-chaconine, have been thoroughly examined for their potential to prevent cancer [81]. Scientists discovered that α-solanine showed growth inhibition and apoptosis induction in several cancer cells, including human colon (HT29) and liver (HepG2) cancer cells [83]. The glycoalkaloids demonstrated anti-proliferative effects on the following human tumor cell lines: cervical (HeLa), liver (HepG2), lymphoma (U937), stomach (AGS and KATO III), and normal liver. The glycoalkaloids exhibited concentration-dependent anti-proliferative actions, with α-chaconine exhibiting more bioactivity than α-solanine. α-Chaconine caused cell death in HT-29 human colon cancer cells by inhibiting the phosphorylation of extracellular signal-regulated kinase and activating caspase-3. α-Chaconine showed strong anti-proliferative properties. Two cell lines that represent prostate cancer, LNCaP and PC3, exhibit characteristics and elevated levels of the cyclin-dependent kinase inhibitor p27. According to more recent reports, α-solanine can effectively suppress the development of pancreatic cancer cells both *in vitro* and *in vivo*. Research has demonstrated that α-solanine inhibits the growth of cancer cells by inducing caspase 3-dependent mitochondrial death [89]. Additionally, cells treated with α-solanine exhibit reduced production of tumor metastasis-related proteins, specifically MMP-2 and MMP-9. α-Solanine stopped the growth of PANC-1, sw1990, and MIA PaCa-2 cells in a dose-dependent way. It also stopped cell migration and invasion at toxic doses. In a xenograft model, α-solanine treatment reduced tumor volume [90]. These investigations have demonstrated beneficial effects on pancreatic cancer both *in vitro* and *in vivo*, potentially mediated by inhibitory mechanisms that may be mediated by inhibiting mechanisms involving metastasis, angiogenesis, and proliferation.

9. Future direction

In developing countries, due to the increasing number of people, food deficiency is a significant issue, and every country is trying to fulfill the food demand. Plant tissue culture has proven to be a valuable technology for improving all crop varieties. Potato is used as a food source, and to enhance potato varieties, tissue culture is best where *in vitro* culturing using a nutrient medium is done. In this technology, potato diseases are dealt with and handled using meristem culture [13] and a large number of potato tubers [91].

Salt is a major abiotic environmental stress, and it affects soil, which is directly related to the productivity of crops. Plants are affected by salt stress, and it is common [92,93]. Plant height, weight production, and different physiological traits are affected by water deficit. Canopy growth in plants is stopped by water deficit stress [34,93,94]. The use of nanoparticles reduces the harmful effects of salt stress, and it increases leaf surface area, plant height, metabolism, and leaf chlorophyll. The best-used nanoparticles are silicon dioxide particles, which increase their absorbance in plants by stomata or roots and decrease the level of sodium ions intake to avoid salt stress [54,95-97]. Silicon nanoparticles are also used to handle water deficit stress in potatoes. They have strong potato plant morphology and metabolism to grow in water-deficit conditions [34,93,98].

10. Conclusion

Potatoes are a significant crop, and they are used as a staple food in many countries where millions of tons of potatoes are produced every year, and many countries are dependent on them**.** It is in the third number after wheat and rice and is an important source of carbohydrates, proteins, and vitamins. Conventional breeding of potatoes does not produce enough potatoes, and it causes pathogens attacks and diseases. Plant tissue culture technology has been proven a promising technology for introducing desired traits in potatoes, as potato is an ideal crop for biotechnology. Tissue culture is a laboratory technology in which potatoes are grown and investigated in a nutrient medium. Abiotic stress also decreases potato production, such as salinity and water deficit conditions. The application of nanoparticles such as silicon dioxide removes the hazardous effect of salinity and water scarcity on potatoes and increases their metabolism and morphology. Plant tissue culture provides and essential medicinal and therapeutic that provide a natural substance to solve the health issue. Further investigation would be recommended.

Disclosure statement

The authors declare no conflict of interest.

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