Review Article

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A comprehensive review on medicinal applications of iodine

https://doi.org/10.1515/revic-2025-0075
Received July 31, 2025; accepted November 22, 2025;
published online December 8, 2025

Abstract: Iodine, an essential trace element, plays a critical role in human health, primarily through its involvement in thyroid hormone synthesis, which regulates metabolism, growth, and neurological development. This research explores the multifaceted medicinal applications of iodine, ranging from its critical role in preventing iodine deficiency disorders, such as goiter and hypothyroidism, to its use in advanced medical therapies. Key areas of focus include radioactive iodine therapy for thyroid cancer and hyperthyroidism, the antimicrobial and antiseptic properties of iodine-based compounds like povidone-iodine, and its significance in pregnancy and fetal development. Emerging research highlights iodine's potential in cancer treatment, dermatology, and reducing oxidative stress. Despite its broad therapeutic utility, challenges such as iodine toxicity and allergic reactions necessitate careful management. This study underscores the importance of balanced iodine intake, advances in iodine-based treatments, and global public health efforts to combat iodine deficiency for improved healthcare outcomes.

Keywords: iodine; medicinal application; biomedicience

1 Introduction

Iodine, a vital trace element, is indispensable for human health due to its central role in thyroid hormone synthesis. These hormones, primarily thyroxine (T4) and triiodothyronine (T3), are crucial regulators of metabolic processes, growth, and neurological development. The human body cannot synthesize iodine; thus, it must be obtained through dietary sources or supplementation. Despite its significance, iodine deficiency remains a global health concern, affecting millions and leading to various health disorders. The primary function of iodine in the human body is to facilitate the production of thyroid hormones. The thyroid gland absorbs iodine from the bloodstream to produce T3 and T4, which regulate numerous physiological processes, including metabolic rate, protein synthesis, and neural development. Adequate iodine levels are particularly critical during periods of rapid growth and development, such as pregnancy and early childhood. Insufficient iodine intake can lead to hypothyroidism, characterized by fatigue, weight gain, and cognitive impairments.[1]

Iodine deficiency is a significant public health issue worldwide. The World Health Organization (WHO) estimates that iodine deficiency affects a substantial portion of the global population, particularly in regions where the soil and water have low iodine content. This deficiency can lead to a spectrum of disorders collectively known as iodine deficiency disorders (IDDs). The most visible manifestation is goiter, an enlargement of the thyroid gland as it attempts to compensate for insufficient hormone production. More severe consequences include cretinism, a condition resulting in severe mental and physical retardation, and various degrees of cognitive impairment in children.[2, 3]

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To combat iodine deficiency, many countries have implemented salt iodization programs, which have proven effective in reducing the prevalence of IDDs. However, changes in dietary habits and the consumption of processed foods, which often use non-iodized salt, have led to concerns about the reemergence of iodine deficiency, even in developed nations. Recent reports suggest that certain populations, including pregnant women and individuals adhering to specific diets, may not be receiving adequate iodine intake, potentially leading to health complications.[4]

Beyond its role in thyroid function, iodine possesses significant antimicrobial properties. Iodine-based compounds, such as povidone-iodine, are widely used as topical antiseptics in medical settings. They are effective against a broad spectrum of pathogens, including bacteria, viruses, and fungi, making them invaluable in preventing infections during surgical procedures and in wound care. The mechanism involves the disruption of microbial cell structures and the inhibition of protein and nucleic acid synthesis.[5]

In nuclear medicine, radioactive iodine isotopes, particularly iodine-131, are utilized in the diagnosis and treatment of thyroid-related conditions. Radioactive iodine therapy is a standard treatment for hyperthyroidism and certain types of thyroid cancer. The thyroid gland's natural ability to concentrate iodine allows for targeted therapy, where radioactive iodine selectively destroys overactive or malignant thyroid tissue while sparing other tissues. This approach has been effective in managing these conditions with relatively few side effects.[6]

Despite its benefits, excessive iodine intake can lead to adverse health effects, including thyroid dysfunctions such as hyperthyroidism or hypothyroidism, and autoimmune thyroiditis. Therefore, maintaining a balanced iodine intake is crucial. The recommended daily allowance varies by age, sex, and physiological status, with increased requirements during pregnancy and lactation to support fetal and neonatal development.[7]

Iodine is an essential element with diverse medicinal applications, primarily centered around its role in thyroid hormone production, antimicrobial properties, and use in medical diagnostics and treatments. Ensuring adequate iodine intake through diet or supplementation is vital for maintaining health and preventing disorders associated with both deficiency and excess. Ongoing public health efforts and research are necessary to monitor iodine nutrition status in populations and to address emerging challenges related to iodine intake.[8]

1.1 Iodine chemistry and biological role

Iodine is a non-metallic element belonging to the halogen group of the periodic table, with the chemical symbol "I" and atomic number 53. This trace element is essential for human and animal life, primarily due to its pivotal role in synthesizing thyroid hormones. The unique chemistry of iodine, including its ability to form a variety of inorganic and organic compounds, underpins its diverse biological functions and applications in medicine and industry.[9]

1.1.1 Chemistry of iodine

Iodine exists in various oxidation states ranging from −1 (iodide, I^-) to +7 (periodate, IO_4^-). The most common forms in biological systems are iodide (I^-) and molecular iodine (I_2). Iodine's high electronegativity and polarizability enable it to participate in redox reactions and form stable covalent bonds. The chemistry of iodine is strongly influenced by its ability to dissolve in both polar and nonpolar solvents, a property that facilitates its interaction with diverse biological molecules.[10, 11]

In aqueous environments, iodine primarily exists as I^- in its reduced form or as I_2 and hypoiodous acid (HOI) in its oxidized states. These forms are highly reactive and capable of modifying biomolecules, particularly proteins, through iodination reactions. This reactivity underlies iodine's antimicrobial and antioxidant properties, which are widely utilized in medical and environmental applications.[12]

1.1.2 Biological role of iodine

1.1.2.1 Synthesis of thyroid hormones

Iodine's most significant biological role is its involvement in the synthesis of thyroid hormones, thyroxine (T4) and triiodothyronine (T3). These hormones are critical regulators of metabolic processes, growth, and neurological development. The thyroid gland actively absorbs iodide from the bloodstream through a sodium-iodide symporter (NIS), incorporating it into the amino acid tyrosine within thyroglobulin to produce T3 and T4. The unique iodine chemistry enables the efficient production of these hormones, which are stored in the thyroid gland and released into the bloodstream as needed.[13]

1.1.2.2 Neurological development and function

Adequate iodine levels during pregnancy and early childhood are critical for brain development. Iodine deficiency during these stages can lead to severe cognitive impairments and developmental disorders such as cretinism. Research highlights that iodine's role in the production of thyroid hormones directly impacts neurogenesis, synaptogenesis, and the myelination of neurons, underscoring its importance in neurological health.[14]

1.1.2.3 Antimicrobial properties

Iodine is renowned for its broad-spectrum antimicrobial properties. Molecular iodine (I_2) and iodine-based compounds, such as povidone-iodine, exhibit bactericidal, virucidal, and fungicidal activity. These compounds disrupt microbial cell walls, denature proteins, and interfere with nucleic acid synthesis. The versatility and effectiveness of iodine-based antiseptics make them indispensable in medical procedures and wound care.[15, 16]

1.1.2.4 Antioxidant Function

In addition to its antimicrobial activity, iodine plays a role as an antioxidant. Iodide scavenges reactive oxygen species (ROS) such as hydrogen peroxide, reducing oxidative stress and protecting cells from damage. This antioxidant function is particularly evident in the thyroid gland, where iodine mitigates the effects of high ROS levels generated during hormone synthesis.[10, 11]

1.1.2.5 Immune system supportno

Iodine has been shown to support immune function by modulating inflammatory responses and enhancing the activity of immune cells. It can influence cytokine production and cellular signaling pathways, contributing to its role in host defense mechanisms.[12]

1.1.2.6 Iodine deficiency and associated disorders

Iodine deficiency remains a significant public health concern worldwide, particularly in regions with low soil iodine content. The World Health Organization (WHO) identifies iodine deficiency as the leading cause of preventable intellectual disabilities globally. Disorders associated with iodine deficiency, collectively termed iodine deficiency disorders (IDDs), include goiter, hypothyroidism, cretinism, and impaired cognitive development. Strategies such as salt iodization and dietary supplementation have been implemented to combat iodine deficiency with considerable success.[13] While iodine is essential for health, excessive intake can also have adverse effects. High iodine levels can disrupt thyroid function, leading to conditions such as hyperthyroidism, hypothyroidism, or autoimmune thyroiditis. The tolerable upper intake level (UL) of iodine varies by age and physiological status, with care needed to avoid exceeding this threshold, especially in vulnerable populations.[15, 16]

Recent studies have explored the role of iodine in non-thyroidal systems, including its potential anti-cancer properties. Research suggests that iodine may influence apoptosis and cell differentiation, particularly in breast and prostate tissues. These findings point to a broader spectrum of iodine's biological roles, which could inform novel therapeutic applications.[10, 11]

Additionally, advancements in iodine supplementation methods, such as iodized oils and biofortification of crops, have enhanced the effectiveness of iodine delivery in deficient populations. These innovations are particularly impactful in addressing iodine deficiency in resource-limited settings.[12]

Iodine is a versatile element with unique chemical properties that underpin its critical roles in human health and disease prevention. Its involvement in thyroid hormone synthesis, neurological development, antimicrobial defense, and oxidative stress reduction highlights its biological significance. Ongoing research continues to uncover new dimensions of iodine's role in health, offering promising avenues for therapeutic applications. While addressing iodine deficiency remains a priority, maintaining balanced iodine levels is equally important to prevent adverse health outcomes.

1.1.3 Physiological significance of iodine

Iodine is an essential trace element crucial for various physiological functions in humans and animals. It plays an integral role in the synthesis of thyroid hormones, which regulate numerous vital processes including metabolism, growth, and neurological development. Iodine is also involved in immune responses and has antimicrobial properties. Understanding its physiological significance involves exploring its influence on the thyroid, brain development, metabolism, and overall well-being.[17]

1.1.3.1 Thyroid Hormone synthesis and metabolism regulation

Iodine's primary physiological function is in the production of thyroid hormones, triiodothyronine (T3) and thyroxine (T4), which are synthesized in the thyroid gland. The process begins with the active transport of iodide ions (I^-) from the bloodstream into thyroid follicular cells. Here, iodide is oxidized to molecular iodine (I_2) and is then incorporated into the amino acid tyrosine within the thyroglobulin protein. This iodinated form of tyrosine is crucial for the production of T3 and T4. These hormones are then released into circulation, where they exert widespread effects on the metabolism of almost every cell in the body.[13]

The thyroid hormones influence metabolic rate, body temperature regulation, and energy production by stimulating mitochondria in cells. They promote protein, lipid, and carbohydrate metabolism, with T3 being more biologically active than T4. Adequate iodine levels are thus required for maintaining normal metabolic function. Iodine deficiency can lead to hypothyroidism, characterized by fatigue, weight gain, and decreased metabolic activity, and is often accompanied by goiter, the enlargement of the thyroid gland due to compensatory hyperplasia.[18]

1.1.3.2 Neurological development and cognitive function

Iodine is essential for the proper development of the central nervous system, particularly during pregnancy and early childhood. Inadequate iodine during these critical periods can lead to severe cognitive impairments. The thyroid hormones, primarily T3, are involved in brain development by promoting neurogenesis, neuronal differentiation, and synapse formation. Furthermore, iodine deficiency during pregnancy has been associated with cretinism, characterized by severe intellectual and developmental disabilities, and is a leading preventable cause of intellectual disability worldwide.[2, 3]

Studies have also shown that iodine deficiency can impair neurocognitive function in children and adults, leading to lower IQ scores and reduced learning ability.[19] This emphasizes the importance of sufficient iodine intake during pregnancy and infancy to avoid irreversible developmental damage.

1.1.3.3 Immune function and antioxidant properties

Iodine contributes to immune system regulation through its antimicrobial and anti-inflammatory effects. Iodide has been shown to modulate the function of immune cells, including T lymphocytes and macrophages. Research suggests that iodine plays a role in maintaining the immune system's homeostasis by influencing the production of cytokines, which are signaling molecules involved in the immune response.[15, 16] Furthermore, iodine has antioxidant properties, which help protect cells from oxidative damage caused by free radicals.

Iodine's antioxidant capabilities are particularly important in the thyroid gland, where oxidative stress is generated during the synthesis of thyroid hormones. Iodide reduces reactive oxygen species (ROS), thereby preventing damage to cellular structures, such as membranes and DNA, which could impair thyroid function.[20, 21] This protective role also extends to reducing systemic inflammation, contributing to iodine's overall support of immune function.

1.1.3.4 Iodine deficiency and its Health implications

Iodine deficiency can lead to a number of health issues, including thyroid dysfunction, developmental abnormalities, and weakened immune response. According to the WHO,[2, 3] iodine deficiency remains one of the most prevalent nutritional deficiencies worldwide, especially in regions where the soil is iodine-deficient or where iodine-rich foods are scarce.

In addition to hypothyroidism and goiter, iodine deficiency during pregnancy can result in congenital anomalies and spontaneous abortion. Furthermore, it contributes to growth retardation in children, adversely affecting bone development and physical growth. Iodine deficiency can also increase susceptibility to infections, as the thyroid hormones are vital for the immune response.[19]

1.1.3.5 Iodine and antimicrobial activity

The antimicrobial properties of iodine are widely utilized in medical and industrial applications. Iodine is a potent antiseptic and is used in iodine-based solutions, such as povidone-iodine, which exhibit bactericidal, fungicidal, and virucidal activity. This ability to kill or inhibit the growth of microorganisms is attributed to iodine's ability to denature proteins and disrupt cellular structures, making it an important agent for wound care, skin disinfection, and sterilization.[15, 16]

Iodine plays a vital role in various physiological functions, with its most critical function being the synthesis of thyroid hormones, which regulate metabolism, growth, and brain development. It is essential for cognitive function, immune system regulation, and antioxidant defense. Iodine deficiency can lead to severe health consequences, including thyroid disorders, developmental delays, and compromised immune responses. Thus, ensuring adequate iodine intake is essential for maintaining health and preventing iodine deficiency disorders. With ongoing research into iodine's broader roles in health, further understanding of its biological significance can help in the development of targeted therapies and public health strategies.

1.1.4 Therapeutic uses of iodine

Iodine is not only an essential trace element for thyroid function but also has a broad range of therapeutic applications in medicine due to its antimicrobial properties, ability to support tissue repair, and role in various treatments. The therapeutic uses of iodine span from its use in disinfectants and wound care to its application in the treatment of certain diseases. This section will explore these uses, including its role in thyroid treatment, infection control, cancer therapy, and as a contrast agent in medical imaging.[17]

1.1.4.1 Thyroid disorders

The most well-known therapeutic use of iodine is in the treatment of thyroid disorders, particularly those related to iodine deficiency. Iodine supplementation is the primary approach to preventing and treating iodine deficiency disorders (IDD) such as goiter and hypothyroidism. The thyroid gland relies on iodine18 to synthesize thyroid hormones (T3 and T4), and a deficiency leads to reduced production of these hormones, resulting in an array of metabolic disturbances [22].

In clinical practice, iodine therapy is used to treat hyperthyroidism (an overactive thyroid), especially with radioactive iodine (RAI) therapy. RAI, administered as an oral dose, is selectively absorbed by the thyroid cells, where it emits radiation that destroys overactive thyroid tissue, thereby reducing hormone production.[23] This non-surgical treatment has been proven to be effective in treating conditions such as Graves' disease, a common cause of hyperthyroidism.

Additionally, iodine is used in the form of potassium iodide in the treatment of thyroid storm, a life-threatening condition characterized by a sudden and severe increase in thyroid hormones, often triggered by infection or surgery.[24] Potassium iodide helps to inhibit the release of thyroid hormones, stabilizing the condition.

1.1.4.2 Antiseptic and antimicrobial properties

Iodine has been utilized for centuries in medical practice, particularly as an antiseptic. The most common form of iodine used for antimicrobial purposes is iodine tincture and povidone-iodine (PVP-I). PVP-I is a broad-spectrum antiseptic that is effective against bacteria, viruses, fungi, and protozoa.[25] It is commonly applied topically for wound cleaning and preventing infections in cuts, abrasions, and burns. The mechanism by which iodine exerts its antimicrobial effects involves the disruption of microbial cell membranes and proteins, leading to the death of pathogens.

Povidone-iodine has gained prominence in the prevention of surgical site infections and is commonly used for preoperative skin disinfection. It also serves in the management of chronic wounds and ulcers, providing an effective means of infection control in diabetic and pressure ulcers.[26] Furthermore, iodine-based antiseptics have been used in the management of oral infections, especially in cases of periodontal disease and mouth ulcers.

1.1.4.3 Cancer therapy

Iodine is also used in the treatment of certain cancers, particularly thyroid cancer. Radioactive iodine (I-131) therapy is a standard treatment for differentiated thyroid cancer (DTC). After surgical removal of the thyroid gland, I-131 is administered to eliminate any remaining thyroid tissue, including cancerous cells. The treatment capitalizes on the thyroid's natural ability to absorb iodine. Once taken up by thyroid cancer cells, radioactive iodine destroys the cancer cells through radiation, effectively preventing recurrence and metastasis.[27]

Moreover, iodine's potential therapeutic application extends to other cancers. Iodine-131 has been explored in the treatment of certain types of lung and ovarian cancers, though these applications are still under investigation. In addition to its radiotherapy use, iodine's ability to influence apoptosis (programmed cell death) is being studied for its potential in enhancing cancer cell response to chemotherapy.[28]

1.1.4.4 Imaging and diagnostic uses

Iodine is extensively used as a contrast agent in medical imaging, particularly in radiological procedures such as X-ray and computed tomography (CT) scans. Iodine-based contrast agents improve the visibility of blood vessels, tissues, and organs in imaging, providing essential diagnostic information. These agents work by absorbing X-rays, which allows for clearer images of internal structures. For instance, in CT scans, iodine contrast agents are injected into the bloodstream to highlight vascular structures and tumors.[29]

Iodine is also used in angiography, a procedure that enables visualization of blood vessels. The iodine contrast helps to identify blockages, aneurysms, and other vascular abnormalities. Iodine-containing contrast agents are critical in the diagnosis of cardiovascular diseases and other conditions requiring detailed imaging.

1.1.4.5 Treatment of radiation exposure

Iodine is used therapeutically in cases of radioactive iodine exposure, a potential risk in nuclear accidents. Potassium iodide (KI) tablets are administered to prevent the thyroid gland from absorbing harmful radioactive iodine. KI blocks the thyroid's ability to uptake radioactive iodine, significantly reducing the risk of thyroid cancer. This form of iodine therapy has been a key element in protective measures following nuclear incidents such as the Fukushima and Chernobyl disasters.[30]

1.1.5 Iodine in antimicrobial applications

Iodine has been a cornerstone in antimicrobial therapy for centuries, owing to its broad-spectrum antimicrobial properties. It is widely used in healthcare settings to prevent and treat infections due to its ability to kill a variety of pathogens, including bacteria, viruses, fungi, and protozoa. The antimicrobial effectiveness of iodine is mainly attributed to its ability to denature proteins and disrupt cell membranes, making it an invaluable tool in both clinical and non-clinical settings. This section explores the various antimicrobial applications of iodine, particularly in wound care, oral health, and infection prevention.[31]

1.1.5.1 Wound care and infection control

Povidone-iodine (PVP-I), a complex of iodine with the polymer polyvinylpyrrolidone, is one of the most commonly used iodine-based antiseptics. Its broad-spectrum antimicrobial activity makes it an ideal agent for cleaning and disinfecting wounds, burns, and cuts. PVP-I is effective against a wide range of microorganisms, including bacteria (both gram-positive and gram-negative), viruses, fungi, and protozoa.[32] It is commonly used in hospitals for preoperative skin disinfection, post-surgical wound care, and in the treatment of chronic wounds such as diabetic ulcers and pressure sores.

The mechanism of action of iodine in wound healing is multifaceted. Iodine penetrates microbial cell walls and disrupts the integrity of the cell membrane, leading to leakage of intracellular contents and ultimately cell death. Additionally, iodine can modulate the immune response by promoting the activity of neutrophils and macrophages, essential cells in wound healing.[33] PVP-I has been shown to accelerate the healing process and reduce the incidence of infection in chronic and surgical wounds. Its use has been associated with a reduction in wound-related complications and improved patient outcomes.

1.1.5.2 Oral health

Iodine is also widely used in oral health products for its antimicrobial properties. It is commonly found in mouthwashes and gargles, where it helps to control oral infections and prevent dental plaque buildup. Povidone-iodine solutions, when used as a mouth rinse, have been shown to reduce the bacterial load in the oral cavity, thereby preventing gingivitis, periodontitis, and other dental infections.[34] It is also effective against viral infections such as herpes simplex virus (HSV) and influenza, commonly seen in the oral mucosa.

One of the advantages of iodine in oral health is its ability to not only reduce the presence of harmful bacteria but also to provide prolonged antimicrobial action. This prolonged antimicrobial effect is beneficial for patients with chronic oral infections or those undergoing dental procedures. Iodine's ability to reduce the incidence of dental caries, gum disease, and oral infections has made it a key component of oral hygiene products.[35] Moreover, iodine-based treatments can aid in preventing post-operative infections after dental surgeries, further showcasing its versatility in oral care.

1.1.5.3 Infection prevention in medical devices

Iodine is increasingly used in the prevention of infections associated with medical devices, including catheters, wound dressings, and prosthetic implants. Medical devices provide a surface for bacterial colonization, increasing the risk of infection. Iodine-coated catheters and surgical dressings help prevent microbial contamination and biofilm formation, which is a key factor in chronic infections.[36] For instance, iodine-coated catheters have been demonstrated to reduce the incidence of catheter-associated urinary tract infections (CAUTI) by effectively inhibiting bacterial growth on the catheter surface.

Iodine-infused wound dressings are also used to prevent infection in chronic wounds, particularly in patients with diabetes or those who have undergone surgery. These dressings slowly release iodine over time, providing continuous antimicrobial protection while maintaining a moist wound environment conducive to healing.[37] Iodine-impregnated medical devices have become an essential tool in infection prevention, especially in immunocompromised patients, where the risk of healthcare-associated infections is higher.

1.1.5.4 Food industry applications

In addition to healthcare and oral health, iodine is used in the food industry as a disinfectant and preservative. Iodine-based sanitizers are widely used to disinfect food contact surfaces, utensils, and equipment. It is effective in reducing microbial contamination, including bacteria such as Salmonella and *E. coli*, which are common causes of foodborne illnesses.[38] Iodine's efficacy in reducing bacterial load on food surfaces helps prevent the spread of infections, ensuring the safety of food products for consumers.

In addition, iodine solutions are used in dairy production, particularly in the sanitization of milking equipment and in controlling the growth of pathogens in milk. The use of iodine in dairy farm practices has been shown to significantly reduce the risk of mastitis, a common infection in dairy cows, while also improving the overall quality of milk production.[39] Iodine's ability to inactivate microorganisms in food processing environments highlights its versatility and effectiveness as a disinfectant across various sectors.

1.1.5.5 Antiviral applications

Beyond its antibacterial activity, iodine also has antiviral properties, which have been increasingly explored in the context of respiratory infections. Iodine solutions, such as povidone-iodine gargles, have shown efficacy in reducing viral loads in the throat, especially in patients with viral infections such as COVID-19.[40] The antiviral action of iodine is attributed to its ability to oxidize and disrupt viral proteins and lipid membranes, rendering the virus inactive. This makes iodine-based products valuable tools in the fight against viral infections, particularly in settings where antiviral drugs are limited or unavailable.

Iodine remains one of the most effective and widely used antimicrobial agents across various fields, including healthcare, oral hygiene, food safety, and medical device infection prevention. Its broad-spectrum activity against bacteria, viruses, fungi, and protozoa has made it indispensable in preventing and treating infections. Povidone-iodine, in particular, has revolutionized wound care, providing a safe and effective means of disinfecting and healing chronic wounds. Additionally, iodine's role in oral health, as well as its potential in controlling viral infections, continues to expand its therapeutic applications. As research continues, iodine's antimicrobial properties are likely to be further explored, offering new possibilities for infection control in both clinical and everyday settings.

1.1.6 Iodine in cancer treatment

Iodine, traditionally recognized for its role in thyroid function, has recently garnered significant attention for its potential applications in cancer treatment. Its role in oncology primarily revolves around targeted cancer therapy, utilizing both its radioactive isotopes and its ability to influence cellular processes, including apoptosis (programmed cell death) and cell proliferation. Iodine's therapeutic potential is particularly highlighted in thyroid cancer treatment, though emerging studies have also shown promise in other cancer types, such as breast, prostate, and liver cancer. This section delves into the different mechanisms and clinical applications of iodine in cancer treatment, focusing on both radioactive and non-radioactive forms of iodine.

1.1.6.1 Radioactive iodine therapy

Radioactive iodine (RAI) therapy is one of the most established and effective treatments for thyroid cancer, particularly for differentiated thyroid cancers (DTC), including papillary and follicular thyroid cancers. The radioactive isotope, iodine-131 (I-131), is preferentially taken up by thyroid cells, making it an ideal therapeutic agent. The radiation emitted by I-131 destroys both cancerous thyroid cells and any remaining normal thyroid tissue following thyroidectomy (surgical removal of the thyroid gland).[41] This targeted radiation therapy has revolutionized the management of thyroid cancer, providing a less invasive and effective alternative to traditional methods such as external beam radiation.

The therapeutic effect of I-131 is attributed to its ability to emit beta particles and gamma rays. Beta particles are capable of causing DNA damage in cancer cells, leading to cell death, while gamma rays can be used for imaging and monitoring therapeutic efficacy. I-131 is particularly effective when used in combination with thyroid hormone withdrawal therapy or recombinant human thyroid-stimulating hormone (rhTSH) to increase iodine uptake by the thyroid cells.[42, 43] Recent studies have highlighted that post-surgical I-131 therapy can significantly reduce the recurrence of thyroid cancer and improve patient survival rates.

1.1.6.2 Iodine in targeted therapy for other cancers

While I-131 is primarily used in the treatment of thyroid cancer, iodine's potential in the treatment of other types of cancer has also been explored. Research is ongoing into the use of iodine in the development of targeted radiopharmaceuticals for non-thyroid cancers, including breast, prostate, and liver cancers. One promising approach involves the conjugation of iodine isotopes to monoclonal antibodies or small molecules that specifically target cancer cell markers. These targeted therapies allow for the selective delivery of radiation to cancer cells, minimizing the damage to surrounding healthy tissue.[44]

In prostate cancer, for instance, iodine-125 (I-125), another isotope of iodine, has been studied for its potential in brachytherapy (a form of internal radiation therapy where a radioactive source is placed directly inside or very close to the tumor). I-125's relatively low-energy radiation is useful for treating localized prostate cancer, offering a treatment option with reduced side effects compared to traditional external beam radiation.[45] Similarly, iodine-based radiopharmaceuticals are being developed for use in other solid tumors, where they can provide targeted delivery of radiation to malignant cells.

1.1.6.3 Non-radioactive iodine in cancer treatment

Beyond its use as a radioactive therapeutic agent, iodine also holds promise in non-radioactive forms for cancer treatment. Iodine has been found to exert various biological effects that can influence cancer cell behavior, including its potential to regulate cell growth and induce apoptosis. Some studies have suggested that iodine supplementation, particularly in the form of iodide, can inhibit the growth of certain cancer cell lines. This effect is thought to be linked to iodine's role in regulating the expression of genes involved in cell cycle control and apoptosis.[46]

Research has shown that iodine can influence the expression of tumor suppressor genes such as p53 and promote the apoptotic pathways in cancer cells. In breast cancer, for instance, iodine has been found to inhibit the growth of estrogen receptor-positive (ER+) cancer cells by modulating the activity of certain enzymes involved in hormone metabolism.[47] Additionally, iodine supplementation has been shown to reduce the proliferation of malignant cells in breast cancer models and increase the sensitivity of these cells to conventional chemotherapies.

Iodine's role in cancer treatment is also being explored in combination with other therapies, including chemotherapy and immunotherapy. Studies have suggested that iodine, when used in conjunction with chemotherapy drugs, may enhance the sensitivity of cancer cells to treatment, improving the efficacy of chemotherapy. This combined approach could lead to a reduction in the required dosage of chemotherapy drugs, potentially reducing the toxic side effects typically a Challenges associated with chemotherapy.[48]

While iodine has shown significant promise in cancer treatment, several challenges remain in optimizing its use in clinical settings. One of the main limitations is the potential for iodine resistance in certain cancer types, where cancer cells may not efficiently uptake iodine or may develop mechanisms to resist the cytotoxic effects of iodine.[42, 43] This highlights the need for ongoing research to develop strategies to enhance iodine uptake or overcome resistance mechanisms.

Moreover, the use of iodine in non-thyroid cancers is still in the experimental stage, and more clinical trials are required to establish the safety and efficacy of iodine-based therapies for other cancer types. Although the combination of iodine with other therapies shows promise, additional studies are needed to determine the optimal dosages and treatment regimens for combined therapy approaches.

1.1.7 Innovative and emerging applications

Iodine, traditionally recognized for its critical role in thyroid function and its use in medical diagnostics and treatments, has seen a rise in innovative and emerging applications across various scientific disciplines. These advancements, particularly in biotechnology, nanotechnology, and environmental science, reflect iodine's versatility as a powerful agent in new therapeutic strategies, diagnostic techniques, and environmental sustainability efforts. This section highlights some of the cutting-edge uses of iodine, exploring its potential in areas such as antimicrobial technologies, medical diagnostics, wastewater treatment, and nanotechnology.[49]

1.1.7.1 Iodine in antimicrobial and antiviral applications

Iodine-based compounds have long been utilized in antiseptics and disinfectants, but recent research has expanded their use in combating microbial and viral infections. Iodine's ability to inactivate a broad range of pathogens, including bacteria, viruses, fungi, and protozoa, is being harnessed in new formulations for medical and public health purposes. One such application is the development of iodine-infused dressings and topical agents for wound care, which has shown promising results in reducing infection rates and accelerating wound healing. In addition, iodine is being incorporated into surgical drapes and wipes to provide long-lasting antimicrobial protection.[50]

More recently, iodine's antiviral potential has garnered attention, especially in light of the COVID-19 pandemic. Studies have shown that iodine-based disinfectants can effectively inactivate the SARS-CoV-2 virus on surfaces and skin, contributing to the reduction of viral transmission.[51] This has led to the development of iodine-based nasal sprays and mouth rinses aimed at reducing viral load in the respiratory tract, presenting a novel preventative measure for respiratory infections.

1.1.7.2 Iodine in nanotechnology and drug delivery

Nanotechnology has enabled significant advancements in the development of novel drug delivery systems, and iodine is increasingly being explored for its potential in this field. Iodine-based nanoparticles have been developed for targeted drug delivery in cancer therapy, particularly in enhancing the delivery of chemotherapy drugs to tumor sites while minimizing systemic toxicity. The ability to modify iodine-containing nanoparticles with targeting ligands allows for highly specific interaction with cancer cells, improving the efficacy of treatment and reducing side effects.[52]

Furthermore, iodine nanoparticles are being studied for their use in imaging and diagnostic applications. Iodine-based contrast agents have been integrated into imaging modalities such as X-ray and computed tomography (CT) scans, enabling enhanced visualization of tissues and organs. Recent developments have led to the creation of iodine-loaded nanocarriers that can be tracked in real-time, providing valuable information for monitoring treatment progress and optimizing therapeutic regimens.

In addition, iodine's unique ability to act as both an antimicrobial and therapeutic agent has been exploited in the development of iodine-based nanocomposites, which possess both antibacterial and anticancer properties. These composite materials are being studied for applications in wound healing, bone repair, and tissue regeneration, offering the potential for multifunctional biomaterials that can address a range of medical challenges simultaneously.[53]

1.1.7.3 Iodine in environmental applications: Wastewater treatment

Iodine is emerging as a valuable tool in the field of environmental sustainability, particularly in wastewater treatment. Iodine's antimicrobial properties make it an effective agent in removing harmful pathogens from wastewater, ensuring that treated water meets safety standards for reuse. Recent research has focused on developing iodine-based materials, such as iodine-infused activated carbon and composites, to improve the filtration and purification of water. These materials work by adsorbing and neutralizing pollutants, including heavy metals, organic contaminants, and pathogens, offering an efficient and environmentally friendly solution to water purification.[10, 11]

Moreover, iodine-based systems are being integrated into decentralized water treatment technologies, where iodine serves as a disinfectant to remove bacteria and viruses in low-resource settings. The ability to produce iodine *in situ*, by electrochemical or photocatalytic methods, has opened up new possibilities for sustainable water treatment systems in rural and underserved areas.[20, 21]

1.1.7.4 Iodine in agricultural and food industries

Another emerging area for iodine application is in agriculture and food safety. Iodine plays a critical role in the growth of crops, particularly in addressing iodine deficiency in soils. Recent studies have shown that iodine fertilization can improve crop yields, enhance plant resistance to pathogens, and increase the nutritional value of food. This has led to the development of iodine-enriched fertilizers, which are being trialed for use in crops such as rice, wheat, and potatoes.[54] These fertilizers not only promote plant growth but also help address the widespread issue of iodine deficiency in populations that rely heavily on crops as their primary food source.

In the food industry, iodine is used as an essential micronutrient for human health, and recent innovations focus on enhancing iodine fortification programs. Iodine-enriched salt and other food products are being developed to combat iodine deficiency disorders (IDD), which are prevalent in many parts of the world. In addition, iodine is being explored as a preservative and antioxidant in food products, offering a natural and safe alternative to synthetic additives.[55]

1.1.7.5 Iodine in diagnostic imaging and molecular imaging

Iodine's role in diagnostic imaging has been significantly enhanced through the development of advanced molecular imaging techniques. Iodine-based compounds are increasingly being used as contrast agents in imaging modalities such as positron emission tomography (PET), magnetic resonance imaging (MRI), and single-photon emission computed tomography (SPECT). These techniques allow for the non-invasive visualization of molecular and cellular processes *in vivo*, which is crucial for early diagnosis and monitoring of diseases such as cancer, cardiovascular disorders, and neurological diseases.[42, 43]

In particular, iodine-131 and iodine-123 isotopes are widely used in nuclear medicine for diagnostic imaging of thyroid diseases, as well as in the evaluation of certain cancers. The emerging trend is the development of iodine-labeled probes that can target specific biomarkers associated with diseases, thereby improving the accuracy and sensitivity of imaging.[56]

1.1.8 Side effects and toxicity

Iodine, a crucial element for human health, particularly for the synthesis of thyroid hormones, is essential in maintaining several physiological processes. However, like many substances, excessive exposure or improper use of iodine can result in adverse effects. Both acute and chronic toxicity can occur due to excessive iodine intake, whether through dietary supplements, pharmaceuticals, or medical treatments. Understanding the side effects and potential toxicity associated with iodine is vital for its safe use in various clinical, diagnostic, and therapeutic applications.[22]

1.1.8.1 Iodine toxicity and overexposure

Excess iodine intake is one of the primary concerns regarding its toxicity. The Recommended Dietary Allowance (RDA) for iodine in adults is 150 µg per day, with upper tolerable intake levels set at 1,100 µg per day. Chronic exposure to iodine levels above this threshold can lead to iodine toxicity, which may manifest through various clinical symptoms.

Ingesting iodine in excessive amounts can lead to iodine-induced thyroid dysfunction, which may include hyperthyroidism or hypothyroidism. The thyroid gland's response to excess iodine is typically to alter the production of thyroid hormones, often leading to thyroiditis, a condition characterized by inflammation of the thyroid gland. These thyroid disruptions can result in symptoms such as fatigue, weight changes, and metabolic disturbances.[24]

Another significant issue related to iodine toxicity is the development of iodine-induced goiter. This condition occurs when the thyroid gland enlarges in response to excessive iodine, as it attempts to compensate for altered hormone production. In some individuals, this may lead to visible swelling in the neck area and difficulty swallowing .

1.1.8.2 Allergic reactions and sensitivities

In addition to systemic toxicity, iodine may cause allergic reactions in sensitive individuals. Hypersensitivity to iodine is relatively rare but can manifest in the form of skin rashes, hives, or more severe conditions like anaphylaxis. An allergic reaction to iodine-based contrast agents used in medical imaging procedures is also a well-known phenomenon, with symptoms ranging from mild itching to severe respiratory distress.

The most common form of iodine allergy involves the use of iodinated contrast media in imaging tests such as CT scans and angiography. These compounds, while generally safe, can provoke an immune response in some individuals, especially those with a known allergy to iodine or shellfish, as both contain similar proteins that may trigger allergic reactions. Reactions can be severe and may include difficulty breathing, swelling, and even anaphylactic shock, requiring immediate medical attention.

1.1.8.3 Iodine poisoning

Acute iodine poisoning occurs when large doses of iodine are ingested, often in the form of iodine-based disinfectants or medications. Symptoms of iodine poisoning include nausea, vomiting, abdominal pain, and diarrhea. In severe cases, acute exposure can lead to shock, organ failure, and death. This form of toxicity is typically associated with accidental or intentional overdoses and requires immediate medical intervention. One of the major concerns regarding iodine toxicity is the potential for iodine burns, especially in the case of topical antiseptics or disinfectants. Prolonged exposure to iodine solutions on the skin can cause irritation, blistering, and tissue damage. For this reason, it is essential to follow proper guidelines when using iodine-containing products in wound care and disinfection.

1.1.8.4 Thyroid cancer and autoimmune disorders

Excessive iodine intake has also been linked to an increased risk of thyroid cancer in certain populations. While iodine deficiency has been historically associated with an increased risk of goiter and thyroid carcinoma, there is evidence that excessive iodine may similarly influence thyroid malignancy.[57] Some studies have suggested that the use of iodine-containing radiopharmaceuticals for diagnostic or therapeutic purposes may contribute to the development of thyroid cancer, particularly when used over prolonged periods.[58]

Additionally, excess iodine intake can trigger autoimmune thyroid disorders, including Hashimoto's thyroiditis (an autoimmune form of hypothyroidism) and Graves' disease (an autoimmune condition leading to hyperthyroidism). These disorders are characterized by the immune system attacking the thyroid gland, leading to chronic inflammation and dysfunction.[10, 11]

1.1.8.5 Iodine deficiency versus excess: The balancing act

It is essential to note that iodine deficiency is equally harmful as excessive iodine intake. Iodine deficiency can lead to goiter, developmental and cognitive impairments in infants and children, and other serious health problems like hypothyroidism. Thus, the goal is to maintain iodine levels within the optimal range necessary for thyroid function while avoiding both deficiency and toxicity.

In areas where iodine deficiency is common, iodine supplementation programs, such as the addition of iodine to table salt, have been instrumental in reducing related health issues. However, iodine fortificaion programs must be carefully monitored to prevent overexposure and toxicity, particularly in regions where iodine deficiency is less prevalent.[28]

1.1.8.6 Precautionary measures and management of toxicity

In clinical settings, healthcare providers often monitor iodine intake, particularly in patients undergoing treatments such as iodine radiotherapy or those with thyroid dysfunction. The management of iodine toxicity typically involves stopping iodine exposure and initiating supportive care, including hydration and the use of medications to stabilize thyroid function. In cases of allergic reactions, antihistamines or corticosteroids may be prescribed, and in severe cases of anaphylaxis, adrenaline is administered. For iodine toxicity due to excess dietary intake or iodine-based products, activated charcoal and gastric lavage are often employed to reduce absorption in severe cases. Regular monitoring of thyroid function through blood tests is also essential to detect early signs of iodine-induced thyroid dysfunction.

1.2 Summary

Iodine is an essential trace element crucial for the production of thyroid hormones, which are key regulators of metabolism and overall growth and development. While iodine deficiency can lead to severe health issues such as goiter, cognitive impairments, and hypothyroidism, an excess of iodine can also result in adverse effects, including thyroid dysfunction, goiter, allergic reactions, and iodine poisoning. The importance of iodine extends beyond thyroid health, as it plays a significant role in medical applications such as antimicrobial treatments, cancer therapies, and emerging technologies in agriculture and environmental management.

2 Recommendations

i. Implement regular screening for iodine levels in populations, especially vulnerable groups, to prevent deficiency and ensure optimal thyroid function.
ii. Train healthcare professionals on the risks of iodine-based treatments and educate patients about potential side effects and the importance of follow-up care.
iii. Ensure proper regulation and dosing of iodine-containing products, like iodized salt and contrast agents, to avoid overexposure.
iv. Promote research into iodine's potential uses in environmental cleanup, sustainable agriculture, and novel medical treatments.

3 Conclusions

Iodine is a vital element with a wide array of physiological, therapeutic, and medical applications. Its role in thyroid hormone production underscores its importance in maintaining metabolic balance and overall health. While iodine deficiency has been historically recognized as a public health issue, excessive iodine intake presents a growing concern, particularly with the widespread use of iodine-based diagnostic and therapeutic agents. The therapeutic benefits of iodine are substantial, from its antimicrobial properties to its effectiveness in cancer treatments. Additionally, the potential for innovative applications in environmental and agricultural sectors further highlights iodine's versatility. However, as with any therapeutic substance, iodine must be used with caution to avoid toxicity. Excessive iodine intake can lead to thyroid disorders, allergic reactions, and, in extreme cases, iodine poisoning.

Acknowledgments: This project was funded by the Deanship of Scientific Research (DRS) at King Abdulaziz University, Jeddah, Saudi Arabia, under grant no. (DRP-23-130-2025). The authors, therefore acknowledge with thanks DSR for technical and financial support.
Research ethics: Not applicable.
Informed consent: Not applicable.
Author contributions: Maaz Khan, and Saidu Nurudeen collect initial data, organized by Khaled Fahmi Fawy. Sudair Ahmad, helped in collection of data along with improvement. Hadi M. Marwani improved the contents. The English language and grammar was improved by Mohmmed M. Rahman. While Ahlam A. Alalwiat, and Majed A. Bajaber organized the data and validation. Hadi M. Marwani, Mohmmed M. Rahman also helped Shahab Khan in revision and finalized the revised the manuscript.
Use of Large Language Models, AI and Machine Learning Tools: In this study various software like Grammarly were used to check grammatical and spelling mistakes by following double human checking.
Conflict of interest: Not applicable.
Research funding: This project was funded by the Deanship of Scientific Research (DRS) at King Abdulaziz University, Jeddah, Saudi Arabia, under grant no. (DRP-23-130-2025). The authors, therefore acknowledge with thanks DSR for technical and financial support.
Data availability: Not applicable.

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