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Recent Studies on Cancer Cell's Inhibition by Organotin (IV) Materials: An Overview

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Abstract

Organotin (IV) compounds have been the focus of recent studies for their potential use in the treatment of cancer. This review provides an overview of recent studies on the inhibition of cancer cells by organotin (IV) materials. The literature suggests that organotin (IV) compounds can selectively target cancer cells and induce apoptosis, making them promising candidates for anticancer drugs. The review covers various types of organotin (IV) compounds, including those containing alkyl, aryl, and amino groups, and their mechanisms of action against cancer cells. Additionally, the study explores the potential toxicity and biocompatibility of these compounds and their derivatives, as well as their potential use in combination therapy. Overall, the results of recent studies suggest that organotin (IV) compounds show great potential for the treatment of cancer. However, more research is needed to fully understand their mechanism of action and potential side effects. The review highlights the need for continued investigation of these compounds and their derivatives to develop effective and safe anticancer therapies.

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1. Introduction

Cancer is a complex disease that arises from uncontrolled growth and division of cells. It is a leading cause of death worldwide, with an estimated 9.6 million deaths in 2018 alone [1]. Despite significant progress in cancer research, the development of effective treatments for many types of cancer remains a major challenge. This has led to increased interest in the search for new and innovative anticancer agents, including organotin (IV) compounds [2,3]. Organotin (IV) compounds have been widely investigated due to their unique physicochemical properties, which make them attractive for a range of industrial applications, including as biocides, stabilizers, and catalysts [4-6]. In recent years, there has been growing interest in the potential use of organotin (IV) compounds as anticancer agents. Studies have shown that organotin (IV) compounds can selectively target cancer cells and induce apoptosis, making them promising candidates for anticancer drugs. Apoptosis, or programmed cell death, is a natural process that occurs in the body to eliminate unwanted or damaged cells. In cancer cells, this process is often disrupted, leading to uncontrolled growth and division [7,8]. Organotin (IV) compounds have been shown to induce apoptosis in cancer cells by various mechanisms, including inhibition of protein tyrosine phosphatases, activation of caspases, and modulation of intracellular signaling pathways. These compounds have also been shown to have synergistic effects when used in combination with other anticancer agents, including chemotherapy and radiation therapy [9].

Despite their potential benefits, there are concerns about the toxicity and biocompatibility of organotin (IV) compounds. Some studies have shown that these compounds can cause toxicity in healthy cells, which could limit their use in clinical settings. However, recent studies have focused on the development of new derivatives of organotin (IV) compounds that exhibit reduced toxicity and improved biocompatibility [10]. This review provides an overview of recent studies on the inhibition of cancer cells by organotin (IV) materials. It covers various types of organotin (IV) compounds and their mechanisms of action against cancer cells. The review also explores the potential toxicity and biocompatibility of these compounds and their derivatives, as well as their potential use in combination therapy. This review aims to highlight the potential of organotin (IV) compounds as a new class of anticancer agents and to provide insight into the challenges that need to be overcome to fully realize their potential.

2. Organotin (IV) Compounds and Their Properties

Organotin (IV) compounds are organometallic compounds that contain a tin atom bonded to one or more organic ligands [11]. These compounds have a diverse range of properties that make them attractive for various industrial applications, including as biocides, stabilizers, and catalysts. One of the key properties of organotin (IV) compounds is their high stability, which arises from the strong bond between the tin atom and the organic ligands. This stability makes them resistant to degradation and makes them effective as preservatives and stabilizers in products such as plastics, paints, and textiles [12]. Organotin (IV) compounds also have unique electronic properties that make them attractive for use as catalysts in a range of organic reactions. The tin atom in these compounds has a vacant d orbital, which can be used to form a bond with a substrate or reagent, allowing for catalytic activity. The published manuscript entitled [13] describes the synthesis and characterization of new organotin (IV) compounds that can be used as effective photo-stabilizers for polyvinyl chloride (PVC) materials. The authors utilized sulfamethoxazole as a ligand to form di-and tri-alkyltin (IV) complexes and evaluated their photo-stabilizing properties using UV-vis spectroscopy, thermogravimetric analysis (TGA), and other techniques as shown in Figure 1. The results showed that the synthesized compounds exhibited excellent photo-stabilizing properties, with some demonstrating higher efficiency than traditional stabilizers. This research provides valuable insight into the potential of organotin (IV) compounds as photo-stabilizers for PVC materials and highlights the importance of ligand design in the development of new and effective organotin (IV) compounds.

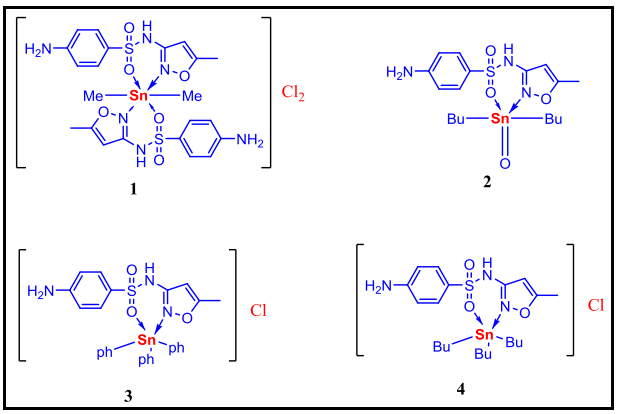

Figure 1. The chemical structure of organotin (IV) compounds 1-4 [13].

In addition to their industrial applications, organotin (IV) compounds have also been investigated for their potential use in medicine. Studies have shown that these compounds can selectively target cancer cells and induce apoptosis, making them promising candidates for anticancer drugs [14]. This selective targeting is thought to arise from the interaction of the organic ligands with specific receptors or proteins on the surface of cancer cells. However, there are also concerns about the toxicity and environmental impact of organotin (IV) compounds. Some of these compounds have been shown to cause toxicity in marine organisms and have been banned for use in certain applications [15]. In general, organotin (IV) compounds have a diverse range of properties that make them attractive for various industrial and medicinal applications. While there are concerns about their toxicity and environmental impact, ongoing research is focused on developing new compounds and derivatives that exhibit reduced toxicity and improved biocompatibility.

3. Inhibition of Cancer Cells by Organotin (IV) Compounds

Organotin (IV) compounds have been investigated for their potential as anticancer agents due to their ability to selectively target cancer cells and induce apoptosis. These compounds have been shown to inhibit the growth of a wide range of cancer cell lines, including breast, colon, prostate, lung, and leukemia [16, 17]. One of the mechanisms by which organotin (IV) compounds induce apoptosis in cancer cells is through the activation of caspase enzymes. Caspases are a family of enzymes that play a key role in apoptosis, and activation of these enzymes leads to the fragmentation of DNA and cell death. Organotin (IV) compounds have been shown to activate caspase-3 and caspase-9 in cancer cells, leading to apoptosis. The published manuscript by Stathopoulou et al. [18] describes the synthesis, characterization, and evaluation of the cytotoxicity of novel organotin derivatives of cholic acid against breast cancer cells. The authors synthesized and characterized several compounds and evaluated their cytotoxicity against MCF-7 breast cancer cells using various assays, including flow cytometry, fluorescence microscopy, and Western blotting. The results showed that the synthesized compounds induced apoptosis in MCF-7 cells by targeting the mitochondria and disrupting their function. The study provides valuable insights into the potential of organotin derivatives of cholic acid as promising anticancer agents and highlights the importance of developing compounds that target specific pathways and cellular components in cancer cells.

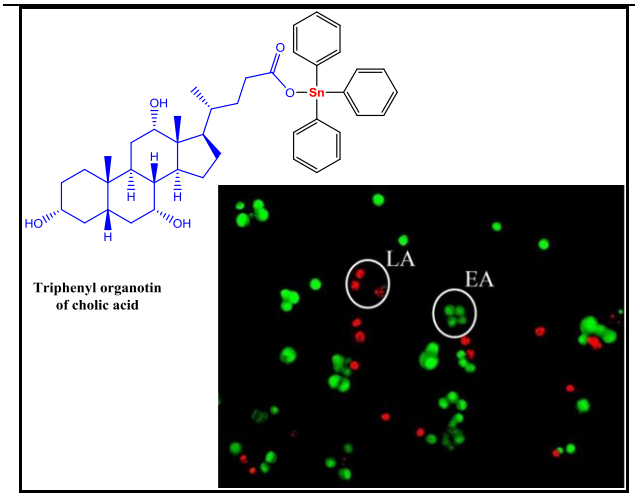

Figure 2. The chemical structure of the cholic acid organotin complex and fluorescence images of the MCF-7 cells incubated with the complex [18].

In addition to caspase activation, organotin (IV) compounds have also been shown to induce cell cycle arrest in cancer cells. Cell cycle arrest is a mechanism by which cells stop dividing and can lead to cell death or senescence. Organotin (IV) compounds have been shown to induce cell cycle arrest at the G2/M phase in cancer cells, preventing their proliferation and growth [19]. Some organotin (IV) compounds have also been shown to inhibit the activity of matrix metalloproteinases (MMPs), which are enzymes that play a key role in cancer metastasis. Inhibition of MMPs can prevent the spread of cancer cells to other parts of the body and can improve the efficacy of cancer treatment [20]. Organotin (IV) compounds have shown promise as potential anticancer agents due to their ability to selectively target cancer cells and induce apoptosis [21]. Further research is needed to develop and optimize these compounds for clinical use, and to address concerns about their toxicity and environmental impact.

4. Mechanisms of Action of Organotin (IV) Compounds in Cancer Cells

Organotin (IV) compounds have been shown to inhibit the growth and induce apoptosis of cancer cells through multiple mechanisms of action. These compounds are known to target different pathways involved in the regulation of cell growth, proliferation, and survival [22]. One of the mechanisms of action of organotin (IV) compounds is the activation of caspase enzymes. Caspases are a family of enzymes that play a key role in apoptosis, and activation of these enzymes leads to the fragmentation of DNA and cell death. Organotin (IV) compounds have been shown to activate caspase-3 and caspase-9 in cancer cells, leading to apoptosis [23]. Organotin (IV) compounds can also induce cell cycle arrest in cancer cells. Cell cycle arrest is a mechanism by which cells stop dividing and can lead to cell death or senescence. Organotin (IV) compounds have been shown to induce cell cycle arrest at the G2/M phase in cancer cells, preventing their proliferation and growth [24].

In 2023 the published paper by Rasli group reports the findings of a study conducted to evaluate the cytotoxicity, apoptosis-inducing potential, and cell cycle arresting properties of a series of organotin (IV) compounds on Jurkat E6.1, T acute lymphoblastic leukemia (T-ALL) cells. The study involved the synthesis of a series of seven organotin (IV) compounds with different dithiocarbamate ligands and their characterization by various spectroscopic techniques as shown in Figure 3. The synthesized compounds were then evaluated for their cytotoxicity against Jurkat E6.1 cells using the MTT assay. The results showed that all of the synthesized compounds exhibited significant cytotoxicity against Jurkat E6.1 cells, with IC50 values ranging from 0.28 to 0.85 µM [25].

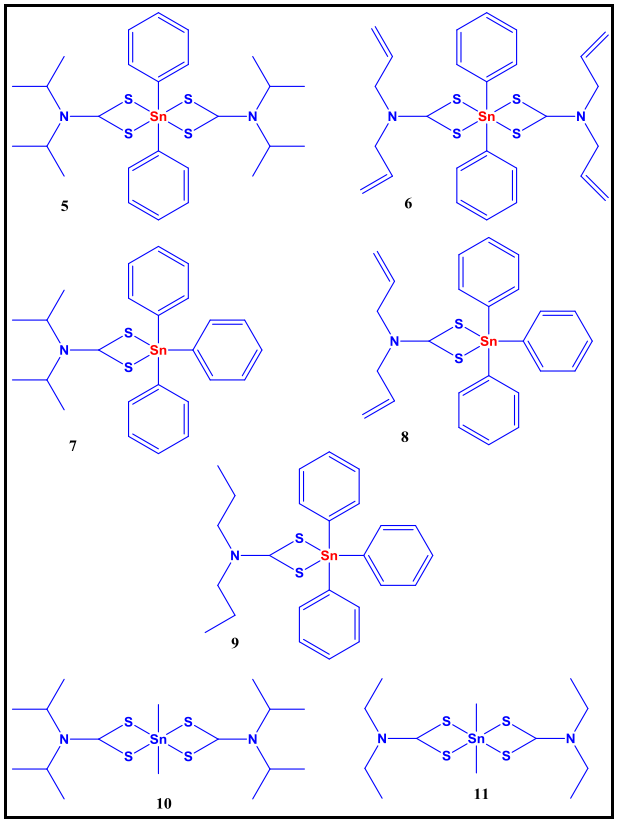

Figure 3. Chemical structures of organotin complexes 5-11 [25].

Further investigation of the mechanism of action of the most active compound was carried out by flow cytometry, DNA fragmentation assay, and Western blot analysis. The results revealed that the compound induced apoptosis in Jurkat E6.1 cells, as evidenced by the increased percentage of cells in the sub-G1 phase, the presence of DNA fragmentation, and the activation of caspase-3 and caspase-9. Additionally, the compound was found to arrest the cell cycle of Jurkat E6.1 cells in the G2/M phase. These findings indicate that the synthesized organotin (IV) compounds have the potential to be developed as anticancer agents for the treatment of T-ALL [25]. Figure 4 depicts the method

by which Jurkat E6.1 cells treated with organotin (IV) dithiocarbamate died. The majority of the cell death that is caused by organotin (IV) dithiocarbamate compounds occurs at the apoptotic phase, with relatively few necrotic populations.

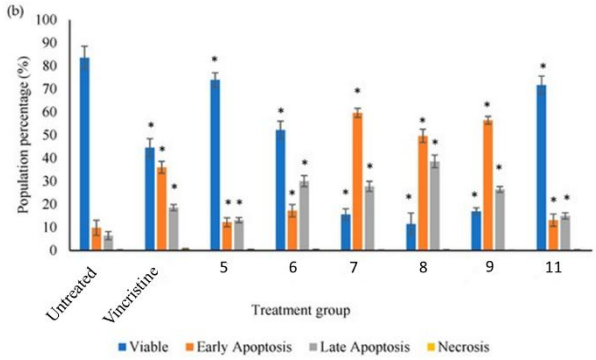

Figure 4. Shows the percentage of viable, early apoptosis, late apoptosis, and necrosis of the death of cancer cells treated with vincristine and organotin complexes 5-11 [25].

In addition to caspase activation and cell cycle arrest, organotin (IV) compounds can also inhibit the activity of matrix metalloproteinases (MMPs), which are enzymes that play a key role in cancer metastasis. Inhibition of MMPs can prevent the spread of cancer cells to other parts of the body and can improve the efficacy of cancer treatment [26]. Organotin (IV) compounds can also induce reactive oxygen species (ROS) generation in cancer cells. ROS are molecules that can damage cellular components, leading to cell death. Organotin (IV) compounds have been shown to induce ROS generation in cancer cells, leading to their death. Moreover, organotin (IV) compounds can also target specific proteins involved in cancer cell survival, such as Bcl-2 and NF-κB. These proteins are overexpressed in many types of cancer and play a key role in cancer cell survival. Organotin (IV) compounds have been shown to inhibit the activity of these proteins, leading to cancer cell death [27]. Organotin (IV) compounds have multiple mechanisms of action in cancer cells, which make them promising candidates for the development of new anticancer drugs. However, further research is needed to better understand the mechanisms of action of these compounds and their potential toxicity in vivo.

5. Toxicity and Biocompatibility of Organotin (IV) Compounds

Although organotin (IV) compounds have shown potential as anticancer agents, their use is limited by their toxicity and biocompatibility issues. These compounds are known to exhibit cytotoxic effects in normal cells, in addition to their anticancer properties, which can lead to unwanted side effects [28]. Organotin (IV) compounds have been shown to affect the function of many different cellular components, including enzymes, DNA, and membrane structures. These effects can disrupt normal cellular processes and lead to cell death or dysfunction. Additionally, organotin (IV) compounds can accumulate in tissues and organs, leading to toxicity and long-term health effects [29]. Furthermore, organotin (IV) compounds can also have negative effects on the environment. These compounds are known to be persistent and can accumulate in aquatic organisms, leading to bioaccumulation and potential environmental harm.

To overcome these issues, efforts have been made to develop organotin (IV) compounds that exhibit lower toxicity and higher biocompatibility. One approach is to modify the structure of these compounds to reduce their cytotoxic effects while maintaining their anticancer properties. Another approach is to develop delivery systems that can target cancer cells specifically, reducing the exposure of normal cells to these compounds [30]. Overall, the toxicity and biocompatibility of organotin (IV) compounds are important considerations in the development of these compounds as anticancer agents. Further research is needed to develop safer and more effective organotin (IV) compounds for clinical use, and to address concerns about their toxicity and environmental impact.

6. Derivatives of Organotin (IV) Compounds for Cancer Treatment

Derivatives of organotin (IV) compounds have been developed to address some of the limitations of these compounds, such as their toxicity and biocompatibility issues. These derivatives can exhibit improved pharmacokinetic and pharmacodynamic properties, leading to increased efficacy and reduced side effects [31].

The paper published by Pantelić et al. presents a comprehensive study on the potential antiproliferative effects of newly synthesized derivatives of organotin (IV) carboxylate compounds as shown in Figure 5 [32]. The research focuses on evaluating the cytotoxicity and growth inhibition properties of these compounds against a panel of human cancer cell lines. The propanoic acid derivatives used in the study were chosen due to their known anticancer activities, and their incorporation into organotin (IV) complexes aimed to enhance their therapeutic potential. The authors performed a series of in vitro experiments, utilizing various techniques such as MTT assay, cell viability assessment, and morphological observations to evaluate the efficacy of the novel compounds [32]. The results demonstrated significant antiproliferative activity against a range of human cancer cell lines, including breast, lung, colon, and prostate cancer. Moreover, the study revealed structure-activity relationships, indicating that specific modifications to the organotin (IV) carboxylate compounds could enhance their potency. The findings presented in this paper provide valuable insights into the development of novel therapeutic agents with potential applications in cancer treatment.

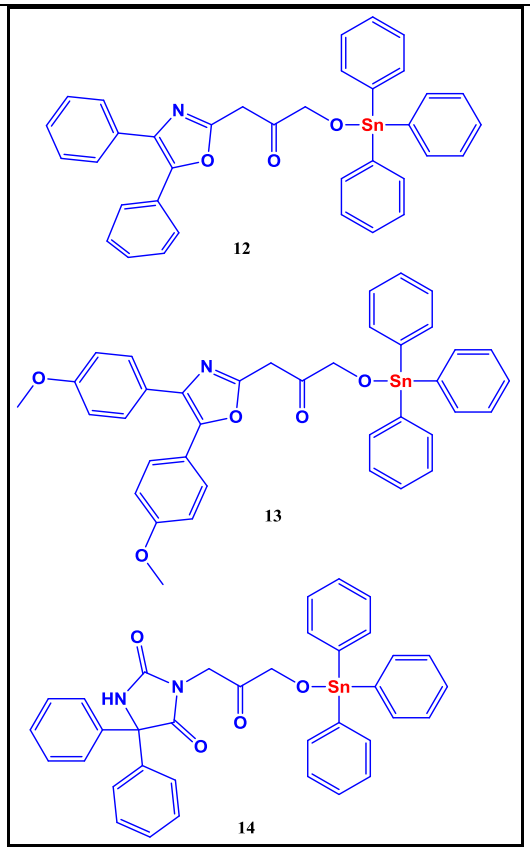

Figure 5. Chemical structure of organotin derivatives 11-14 [32].

One approach to developing derivatives of organotin (IV) compounds is to modify their structure. This can involve adding functional groups to the compound or altering its chemical structure to improve its properties. For example, some derivatives have been developed that exhibit higher water solubility, which can improve their bioavailability and reduce toxicity [33]. Another approach is to develop targeted delivery systems for organotin (IV) derivatives. These systems can be designed to specifically target cancer cells, reducing exposure to normal cells and potentially reducing side effects. Targeted delivery systems can include nanoparticles, liposomes, or other drug delivery systems that can deliver the organotin (IV) derivative directly to cancer cells. Some studies have reported promising results for derivatives of organotin (IV) compounds in preclinical studies. For example, some derivatives have been shown to exhibit higher anticancer activity and lower toxicity compared to the original compound. However, further research is needed to evaluate the safety and efficacy of these derivatives in clinical studies [34]. In general, derivatives of organotin (IV) compounds offer a promising approach to improving the therapeutic potential of these compounds for cancer treatment. Further research is needed to optimize the structure and delivery systems of these compounds and to evaluate their potential for clinical use.

7. Conclusion and Future Directions

In conclusion, organotin (IV) compounds have shown promising anticancer activity through multiple mechanisms of action. While their use has been limited by concerns regarding toxicity and biocompatibility, several approaches have been explored to address these issues. Derivatives of organotin (IV) compounds and combination therapy with other agents have both shown potential in preclinical studies. Future research directions in this field include optimizing the structure and delivery of organotin (IV) compounds and their derivatives to increase their efficacy and reduce toxicity. Additionally, further investigations are needed to explore the potential of combination therapy with organotin (IV) compounds and other agents, including immunotherapy and targeted therapies. In addition to further preclinical and clinical research, there is a need for more detailed studies of the underlying mechanisms of action of organotin (IV) compounds in cancer cells. These studies will help to guide the development of more effective therapies and improve our understanding of how these compounds can be used to treat cancer. To summarize, organotin (IV) compounds offer a promising approach to cancer treatment, and continued research in this field has the potential to lead to the development of novel and effective therapies for a range of cancers.

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