Al-Rafidain J Med Sci. 2023;5:50-56.
DOI: https://doi.org/10.54133/ajms.v5i.146

AJMS
Online ISSN (2789-3219)

Review Article

Organotin(IV) Complexes as Promising Potential Drug Candidates in the Field of Cancer Chemotherapy: A Narrative Review

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Received: 9 June 2023; Revised: 12 July 2023; Accepted: 15 July 2023

Abstract

Organotin(IV) complexes have a wide range of different applications. They are highly involved in pharmaceutical applications and have shown anticancer activity against various cancer cell lines. They act as antioxidants and can scavenge free radical species. The biological activity of organotin complexes depends on the organic moiety, type of substituents, number, type, and content of heteroatoms, and their geometry. The current review aimed to discuss using organotin complexes against different cancer cells.

Keywords: Organotin(IV) complexes, Cephalexin, Anticancer activity, Antioxidants, Medicinal and pharmaceutical applications.

معقدات القصدير العضوي الرباعية كمرشحات محتملة واعدة للأدوية في مجال العلاج الكيميائي للسرطان: مراجعة سردية

الخلاصة

تحتوي مجمعات القصدير العضوي الرباعية على مجموعة واسعة من التطبيقات المختلفة. إنها تشترك بشكل كبير في التطبيقات الصيدلانية وأظهرت نشاطا مضادا للسرطان ضد خطوط الخلايا السرطانية المختلفة. أنها بمثابة مضادات الأكسدة ويمكن أن تفترس أنواع مختلفة من الجذور الحرة. يعتمد النشاط البيولوجي لمعقدات القصدير العضوي على الشقوق العضوية، ونوع البدائل، وعدد ونوع ومحتوى الذرات غير المتجانسة، وهندستها. تهدف المراجعة الحالية إلى مناقشة استخدام مجمعات القصدير العضوي ضد الخلايا السرطانية المختلفة.

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Article citation: ErfanA, Yousif E, Alshanon A, Ahmed DS, Bufaroosha M, El-Hiti G. Organotin(IV) complexes as promising potential drug candidates in the field of cancer chemotherapy: A narrative review. *Al-Rafidain J Med Sci*. 2023;5:48-56. doi: https://doi.org/10.54133/ajms.v5i.146

INTRODUCTION

Diethyltindiiodide was the first organotin compound that Edward Frankland discovered in 1849. There are large numbers of organotin(IV) compounds (based on the organic group) that have been used in various fields such as industry, pharmaceuticals, stabilizers, fire retardants, fungicides, and bactericides [1]. From the 1950s onward, organotin(IV) carboxylate complexes became more important when the polyvinyl chloride (PVC) industry expanded. The most attention was paid to studying organotin(IV) complexes due to their industrial and biological applications against bacterial, fungal, and cancer cell lines [2]. In the Periodic Table, tin is located in Group 14 with the electronic configuration [Kr] $4d^{10}5s^25p^2$; despite the fact that tin has two main oxidation states, $^+2$ and $^+4$, it is rapidly oxidized to tin(IV). It has 10 stable isotopes, considered the largest number compared with the other elements. In the technique of NMR spectroscopy, the isotopes used are ^{117}Sn and ^{119}Sn with spin 1/2 [3,4]. Both

tin(II) and tin(IV) compounds have structures that differ in the coordination sphere depending on the coordination number, with tin (II) in bent, pyramidal, or distorted form and tin(IV) in tetrahedral, bipyramide, or octahedral form. All outer electrons in tin(IV) compounds participate in bonding, but those in tin (II) compounds are not because they have only one electron pair [4]. The organic ligands contain electron-rich atoms such as nitrogen, oxygen, sulfur, and phosphorous, and when bonding with tin, a wide group of stable complexes is formed, and the activity of these compounds is dependent largely on the types and numbers of R groups attached to tin [5]. Organotin(IV) compounds contain one or more direct covalent bonds between C atoms of the organic group that bond to a tin atom. Organometallic compounds, especially organotin compounds, have many applications [6,7]. The organotin halides have a hydrolysable nature, and they are used as starting materials. The complexes synthesized from them are prepared in anhydrous organic solvents such as benzene, acetone, methanol, and ethanol [8]. Organotin(IV) carboxylates can adopt various structures based on the nature and organic groups at tin and carboxylate ligand R'COO in amino acids and peptides. Both O- and N-functional groups make these carboxylate ligands distinctive, and it is important to study the ability of the organotin moiety to bind with the protein constituents and their effect on structures [9].

Industrial preparation of organotin compounds

The metal and alkyl or aryl halide are used to prepare the Grignard reagents (RMgX), but this is an expensive process because it causes waste in the quantities of solvents used and because it's not easy to restrict its reaction with $SnCl_4$ to partial alkylation, except if R is very bulky. The reaction is complete to give R_4Sn, as shown in the following equations, where R is an alkyl or aryl group. Then, the Kocheshkov reaction occurs, where tetra-alkyl stannane is heated with a suitable amount of $SnCl_4$, and redistribution occurs to give the alkyltin chlorides R_nSnCl_{4-n}. Ladenburg discovered the Wurtz reaction in 1871 who prepared phenyltriethyltin by refluxing an ethereal solution of triethyltin iodide and bromobenzene with sodium. In 1947, he patented the preparation of tetraphenyltin from stannic chloride, chlorobenzene, and sodium in boiling benzene, as shown in the equation below:

$$4BuCl + SnCl_4 + 8Na \longrightarrow Bu_4Sn + 8NaCl$$

The industrial preparation of dibutyl and dioctyltin dichloride is shown below. These organoaluminium compounds react with $SnCl_4$ to give the corresponding alkyltin chlorides, and the reaction gives the alkyltin halides directly in the stage of partial alkylation, as described in the following equation:

$$2Bu_3Al + 3SnCl_4 \longrightarrow 3Bu_2SnCl_2 + 2AlCl_3$$

The tetraorganotin is prepared by reacting organoaluminium compounds with stannic chloride in the presence of ether as a complexing agent to increase the efficiency of the reaction without a solvent's presence [6,7,10-13].

$$3SnCl_4 + 4R_3Al \longrightarrow 3R_4Sn + 4AlCl_3$$

Organotin derivatives as anti-cancer agents

Although cisplatin (Figure 1) is the most effective anticancer agent, its primary nephrotoxicity and increased tumor resistance have led to the development of platinum and non-platinum metal complexes with comparable anticancer activity. Organotin(IV) compounds showed significant anticancer activity *in vitro* in various cancer cell lines. These compounds have a distinctive stereochemical perspective and showed great effect as anticancer agents and other proliferative diseases because they interact with the phosphate group of DNA. In addition, the coordinated ligand affects the activity and structure of organotin(IV) compounds [14,15].

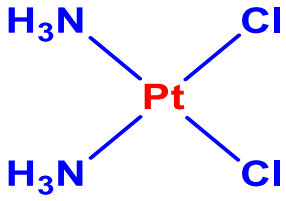

Figure 1: The platinum complex (Cis-platin) [18].

The backbones of DNA sugar are phosphate groups that are considered anchoring sites, and the nitrogen that binds to the DNA base plays the main role in the effectiveness and stability of the tin central atom in octahedral geometry. Organotin complexes, like most anticancer drugs, have anticancer activity that increases with increasing doses because they act on the gene in the tumor cells [17]. Organotin derivatives follow different mechanisms to cause direct damage to the DNA because this derivative has cytotoxic and anticancer activity. Some of these mechanisms are: increasing the Ca^{2+} concentration, which leads to apoptosis; inhibiting the main macromolecule formation; peroxidation of linoleic acid; and mitochondrial metabolism [18]. The tests of organotin(IV) compounds show different results as anticancer activities because some of these compounds have effects on the cancer cell lines while others do not, and this means there are different mechanisms of organotin(IV) compounds depending on the R-groups in the ligand that is used [19]. The anticancer activities of organotin(IV) complexes are affected by several factors, such as the nature of R-groups on Sn and carboxylate ligands, which may be hydrophilic or lipophilic, facilitating the transportation of complexes across the membranes of cells. The number and nature of substitution groups of the same ligand affect its toxicity: R3Sn > R_2Sn > RSn, and the different cancer cell lines [20]. In malignant cells, the first

phase of the eukaryotic cell cycle for this period is called the G1 phase or Gap 1 (which happens before the step of DNA replication), where the size of cells and numbers of proteins, mitochondria, and ribosomes increase. DNA replication starts after that and during the synthesis phase (S). The next step is the synthesis of proteins and growing the cells, called the G2 phase or Gap 2. After that, the mitosis stage (M) occurs, where the separation of chromosomes occurs in the cell nucleus into two identical groups in two nuclei. The final step is the G0 phase, in which the dividing of the cell stops, and the cell gets out of the cell cycle. As a result, the anticancer drugs in cancer cells inhibit cell growth and lead to apoptosis [21]. Several studies have tested the effectiveness of organotin(IV) complexes with different ligands as anticancer drugs for different types of cancer cell lines. Min Hong *et al.* (2013) prepared four organotin(IV) complexes, which are $(CH_3)_2SnC_{18}H_{11}N_2O_3Cl$ (complex 1), $(C_6H_5)_2SnC_{18}H_{11}N_2O_3Cl$ (complex 2), $(o\text{-}Cl\text{-}C_6H_4CH_2)_2SnC_{18}H_{11}N_2O_3Cl$ (complex 3), and $[(C_4H_9)_3Sn(C_{18}H_{11}N_2O_3Cl)]_n$ (complex 4), and their structure was studied using FT-IR, NMR, and XRD analyses. Also, their efficiency as anticancer agents has been tested on these types of human colon cancer cells (HCT-8), lung cancer cells (A549), and human pro-myelocytic leukemia cells (HL-60) by MTT assay. For all complexes, the central (tin) atom is coordinated with the enolic tridentate ligand in the ONO chelate mode in trigonal bipyramidal. Still, in the case of tri-n-butyltin, part of it is bridged by the O atom de-protonation of phenolate and the C=O from the non-enolic modified ligand. Based on previous research results, the inhibition percentage is directly proportional to the increase in organotin IV complex concentration. The IC_{50} results of Complex 4 (with the longest carbon chain) show high efficiency against the three types of cancer compared to other complexes (1-3) and complex structures shown in Figure 2 [22].

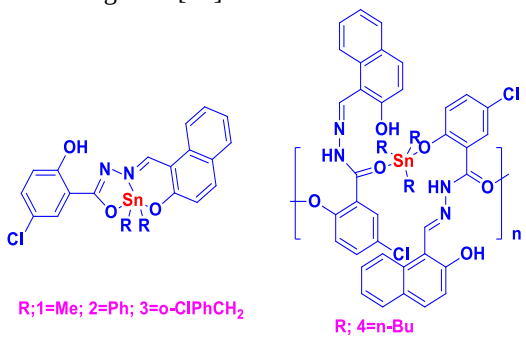

Figure 2: The structures of complex 1: $(CH_3)_2SnC_{18}H_{11}N_2O_3Cl$, complex 2: $(C_6H_5)_2SnC_{18}H_{11}N_2O_3Cl$, complex 3: $(o\text{-}Cl\text{-}C_6H_4CH_2)_2SnC_{18}H_{11}N_2O_3Cl$ and complex 4: $[(C_4H_9)_3Sn(C_{18}H_{11}N_2O_3Cl)]_n$ [22].

A group of researchers, Christophe Nguyen *et al.* (2021), prepared two complexes, AuP-$SnPh_2$ (gold porphyrin with tin(IV) cations connected by malonate and two phenyl ligands) and AuP-Sn_2Ph_6 (two tin(IV) cations chelated to COOH of malonate and three phenyl ligands) (they are called complex no. 1 and 2, respectively) (Figure 3) and characterized by IR and ^{119}Sn NMR. The results show that in the solid state, the tin is five-coordinated and bridging to two various malonate units. While the tin in solution is tetracoordinate and in monomeric form. The complexes are evaluated as anticancer on MCF-7 and healthy cell lines (FS 20–68) and show activity against them because of the covalent bond between the organotin complexes and gold porphyrin [23].

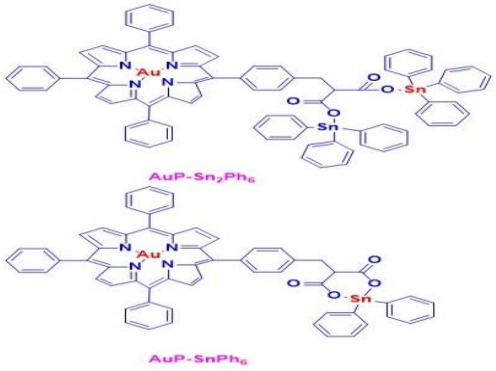

Figure 3: The two synthesized complexes, complex (1): AuP-$SnPh_2$ and complex (2): AuP-Sn_2Ph_6 [23].

Al-Rikabi *et al.* (2023) prepared two organotin carboxylates [Ph_3SnL complex (1) and Me_2SnL_2 complex (2)] (Figure 4) by using Ph_3SnCl and Me_2SnCl_2 salts with 2-[(2,3-dimethylphenyl) amino] benzoic acid as ligand, and both complexes were evaluated for their structure by FTIR and NMR; the activity of the two complexes against the target cell line (A-172) was compared with the original ligand, and the organotin complex showed that it has higher cytotoxicity. The effectiveness of Me_2SnCl_2 (higher anticancer activity) is attributed to the presence of methyl groups, symmetry, and higher tin content [24].

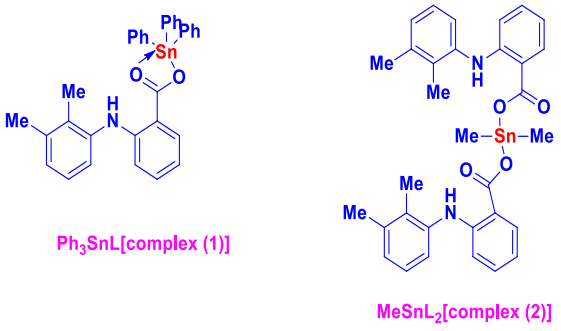

Figure 4: The di and tri-organotin carboxylate [Ph_3SnL complex (1) and Me_2SnL_2 complex (2)] where the ligand is 2-[(2,3-dimethylphenyl)amino] benzoic acid [24].

Eight diorganotin complexes have been synthesized by LIU et al. (2019) with salicylaldehyde thiosemicarbazone as a ligand and studied by ^1H and ^{13}C NMR, IR, elemental analysis, and XRD. The eight complexes are coded as A, B, C, D, E, F, G,

and H. The structure details are explained in Figure 5. The results showed that all complexes have a heterocyclic structure with a five- or six-membered ring. These complexes were evaluated for their anticancer activity against several types of cancer cells (MDA-MB-231 and MCF-7) and demonstrated high activity. The activity of complexes showed a high inhibition percentage against breast cancer cells with increasing complex concentration and based on the longer-chain hydrocarbon [25].

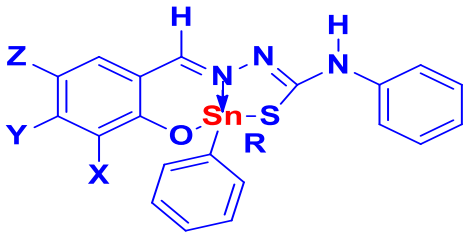

Figure 5: The eight diorganotin (IV) complexes that synthesized with salicylaldehyde thiosemicarbazone as a ligand [25].

In another study, two organotin complexes $(C_6H_5)_2Sn[S_2CN(C_3H_5)_2]_2$ (complex 1) and $(C_6H_5)_3Sn[S_2CN(C_3H_5)_2]$ (complex 2) (Figure 6) were prepared by Haezam *et al.* (2021) from organotin(IV) and diallyldithiocarbamate as ligands. The complexes were characterized by several techniques, such as CHN and S analysis, FTIR, ^{1}H, ^{13}C, and ^{119}Sn NMR, and evaluated for their anticancer activity in several cancer cell lines. The results showed that the coordination of $(C_6H_5)_2Sn[S_2CN(C_3H_5)_2]_2$ is six while the coordination of $(C_6H_5)_3Sn[S_2CN(C_3H_5)_2]$ is five, and both complexes are crystallized in monoclinic. Based on their structures, properties, and R groups, the cytotoxicity results differ for the two complexes [26].

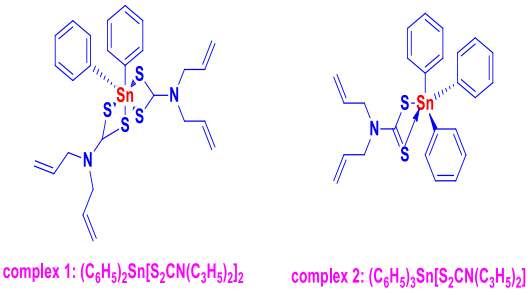

Figure 6: The structures of the two organotin complexes, complex (1): $(C_6H_5)_2Sn[S_2CN(C_3H_5)_2]_2$ and complex (2): $(C_6H_5)_3Sn[S_2CN(C_3H_5)_2]$ with diallyldithiocarbamate as ligand [26].

Also, Xiaoa *et al.* (2013) prepared two organotin complexes, which are [complex (1): $(TolSnOL_1)_6$] and [complex (2): $(TolSnOL_2)_6$] from di(p-methylphenyl) oxide (Tol_2SnO) by using two ligands. 3-(1,3-Dioxo-1H,3H-benzo[de]isoquinolin-2-yl)-propionic acid and 3-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-propionic acid are diagnosed by the following techniques: IR, ^{1}H, ^{13}C, and ^{119}Sn NMR. The results explained that the coordination of both complexes was bidirectional. Evaluation of synthesized organotin(IV) complexes exhibits high anticancer effects against three types of cancer cells [27]. From tri-organotin(IV) compounds, Pantelić *et al.* (2020) synthesized two organotin complexes [Ph_3SnL_1 and Ph_3SnL_2] (Figure 7) by using two different ligands, the first 2-(5-(4-fluorobenzylidene)-2,4-dioxotetrahydrothiazole-3-yl) propanoate (complex 1) and the second 2-(5-methyl-2-furylidene)-2,4-dioxotetrahydrothiazole-3-yl) propanoate (complex 2) and identified by several techniques such as FTIR and NMR.

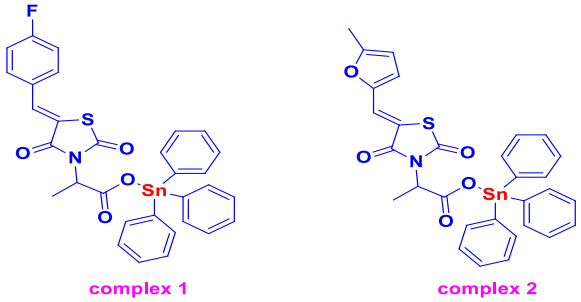

Figure 7: The structures of two organotin complexes, Ph_3SnL_1 (complex 1) and Ph_3SnL_2 (complex 2) where L_1 and L_2 are different ligand [28].

Both complexes were tested against the prostate cell line PC-3, and complex (1) showed the highest anticancer activity and cell growth inhibition compared to cisplatin and other cancer cell lines [28]. Five new organotin complexes were reported by Antonenko *et al.* (2023), which are (1) Me_2SnL_2, (2) Bu_2SnL_2, (3) Ph_2SnL_2, (4) Ph_2SnL_2, and (5) Ph_3SnL_2. The ligand is 2-(N-30,50-di-tert-butyl-40-hydroxyphenyl)-iminomethylphenol, and all synthesized complexes are studied by IR, ^{1}H, ^{13}C, ^{119}Sn NMR, ESI-MS, elemental analysis, and XRD. The results explained that both complexes contain two types of H-bonding (intramolecular and intermolecular), and the complex (2) structure has a distorted octahedral form around the Sn center. All five complexes are tested for their anticancer activity against four types of human cancer cell lines. Based on several factors such as polymerization, the influence of Tb+MAP, and the nature of the R groups, the reported cytotoxicity of organotin complexes decreases in this order: n-Bu > Ph, Et > Me, and 2 and 5 complexes demonstrated high anticancer activity against the cell lines [29]. Dahmani *et al.* (2020) used both piperic and phenylthioacetic acids to synthesize new organotin complexes, which are $\{[n\text{-}Bu_2SnO_2C\text{-}(CH{=}CH)_2\text{-}C_7H_5O_2]_2O\}_2$, $\{[n\text{-}Bu_2SnO_2C\text{-}CH_2\text{-}S\text{-}C_6H_4]_2O\}_2$, and $[Ph_3SnO_2C\text{-}(CH{=}CH)_2\text{-}C_7H_5O_2]_n$; these complexes have been numbered (1, 2, and 3, respectively) (Figure 8) to distinguish them from the rest of the complexes in this review. Several techniques have been used to study these complexes, including IR, NMR, and XRD, which showed that both complexes (1 and 2) are triclinic systems. In contrast, complex (3) crystals are a monoclinic system. All three

complexes were evaluated as anticancer agents against many cancer cell lines. The inhibitory activity of complexes (1 and 2) showed good activity, while complex (3) showed poor activity, which may be due to the presence of three phenol groups (bulky groups) [30]. Panteli´c *et al*. (2021) prepared several organotin(IV) complexes (Ph_3SnL_n) coded with the numbers (1, 2, and 3) (Figure 9) using three different ligands, which are 3-(4,5-diphenyloxazol-2-yl) propanoic acid, 3-(4,5-bis(4-methoxylphenyl) oxazol-2-yl) propanoic acid, and 3-(2,5-dioxo-4,4-diphenylimidazolidin-1-yl) propanoic acid, respectively.

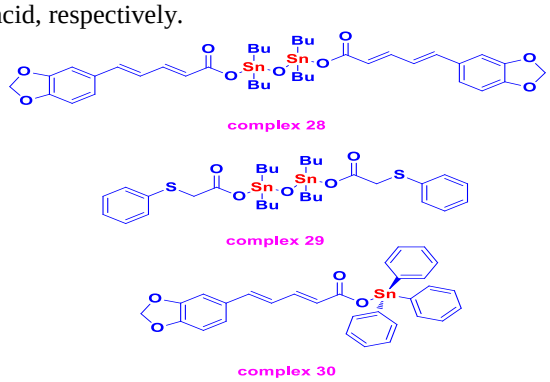

Figure 8: The structures of the organotin (IV) complexes which are; complex (1): $\{[n\text{-}Bu_2SnO_2C\text{-}(CH{=}CH)_2\text{-}C_7H_5O_2]_2O\}_2$, complex (2): $\{[n\text{-}Bu_2SnO_2C\text{-}CH_2\text{-}S\text{-}C_6H_4]_2O\}_2$ and complex (3): $[Ph_3SnO_2C\text{-}(CH{=}CH)_2\text{-}C_7H_5O_2]_n$ [30].

The three complexes (1-3) were evaluated against several cancer cell lines by MTT assay. The results showed that all three complexes exhibited good anticancer activity against all cell lines except complex (3), which showed the highest anticancer activity against HepG2 hepatic cell lines. In contrast, complex (1) exhibits the highest anticancer activity toward MCF-7 breast cancer cell lines. The researchers explained that the organotin(IV) compounds affect the metabolic pathways of the cancer cells [31].

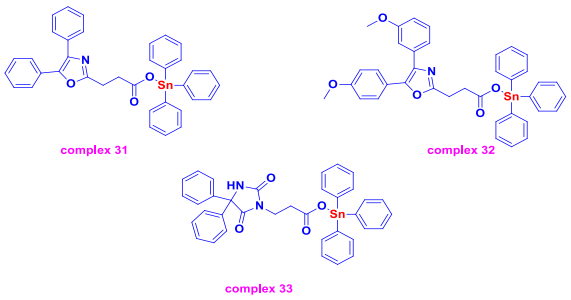

Figure 9: The three organotin complexes synthesized (Ph_3SnL_n); complex(1): Ph_3SnL_1, complex(2): Ph_3SnL_2 and complex(3): Ph_3SnL_3 [31].

Baul *et al*. (2022) used 2-((E)-(4-hydroxy-3-((E)-((4-(methoxycarbonyl) phenyl) imino) methyl) phenyl) diazenyl) benzoic acid as ligands. They synthesized three organotin(IV) complexes coded as (1, 2, and 3), which are $[Bu_3Sn(L)]_n$, $[Ph_3Sn(L)]_n$, and $[n\text{-}Bu_2Sn(L)_2]_2$, respectively. These complexes were characterized by elemental analysis, IR, ^1H, ^{13}C, ^{119}Sn NMR, and X-ray diffraction analysis. The results demonstrated that the tin center in both complexes (1 and 2) is distorted in trigonal bipyramidal geometry (pentacoordinated). In contrast, the tin center in complex (3) is distorted in pentagonal bipyramidal coordination geometry (heptacoordination). All three complexes are evaluated for their anticancer activity of cancer cell lines. The complexes (1 and 2) showed the highest anticancer activity; they contained diazenyl- and imino-groups that improved their cytotoxicity [32]. Kamaludin *et al*. (2019) prepared two organotin(IV) complexes: diphenyltin(IV) (2-methoxyethyl) methyldithiocarbamate, which coded as number (1), and triphenyltin(IV) (2-methoxyethyl)methyldithiocarbamate which coded as number (2) (Figure 10). Their cytotoxicity was evaluated against the K562 cell line. The results of IC_{50} explained that both complexes (1 and 2) have high activity against this cancer cell line and are directly proportional to an increase in the concentration of these complexes [33].

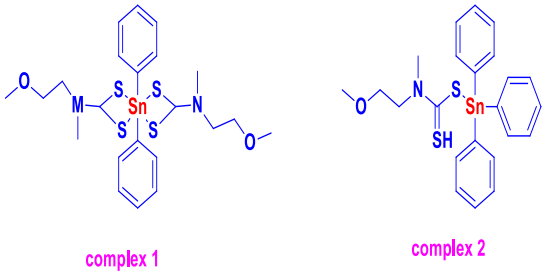

Figure 10: The structures of two novel organotin (IV) complexes; complex (1): diphenyltin (IV) (2-methoxyethyl) methyldithiocarbamate and complex (2): triphenyltin (IV) (2-methoxyethyl) methyldithiocarbamate [33].

Organotin derivatives as antioxidant agents

The antioxidants prevent cell damage by a sequence reaction such as peroxidation of lipids or DNA and protein oxidation. Damage to DNA causes mutations or cancers, while protein damage causes enzyme inhibition, denaturation, and protein degradation [34]. Antioxidants act to decrease the damaging effects of oxidants by donating one electron to the oxidant compound, which inhibits its activity. As a result, many diseases, such as aging, cardiovascular disease, diseases related to the skin, and malaria, are inhibited. So work was being done on developing organotin(IV) compounds for metal-based antioxidant drugs [35]. The antioxidant compounds act by scavenging the free radicals in the cells, preventing damage to healthy cells, and maintaining the oxidation/reduction reactions in the cells. In general, the pH of the healthy cells is about 7.4, and the antioxidants reduce the free radicals, such as the phenolic hydroxide group, by protonation in acidic media without affecting the healthy cells, reducing

the compounds' toxicity [36]. Most reports indicate that three vitamins are very active as antioxidants: C, E, and K because they decrease or stop the development of different types of cancer. Also, 2,6-di-tert-butylphenols tend to form stable radicals of phenoxyl and are considered active antioxidants, so when these fragments are present in organotin complexes, it makes them have anti-radical properties. It makes these complexes safer against normal cells [37]. The biological activity of organotin(IV) compounds depends on the changes of the alkyl substituents on them, where the Sn bonds with the SH group on the protein, leading to oxidative stress activation and cell damage in the organism. Living organisms are exposed to oxidation with oxygen in the atmosphere, so antioxidants preserve these organisms and act to maintain more products such as petrochemicals, polymers, meals, and cosmetics [38]. One of the mechanisms to induce apoptosis is to increase oxidative stress by producing a certain amount of reactive oxygen species (ROS) that devastate the cells via chain radical reactions [36]. Several methods study the antioxidant activity of complexes. The most widely used method is the DPPH assay, which is a 2,2-diphenyl-1-picrylhydrazyl stable radical compound, and by adding hydrogen atoms to it, the violet color of the DPPH radical changes to a stable pale yellow when it reacts with an antioxidant complex (Figure 11) [29]. The antioxidant activity of this method is measured by using a UV-Vis spectrophotometer at the wavelength (515–520 nm), so it gives information about the antioxidant capacity to donate the H atom to the complex [39].

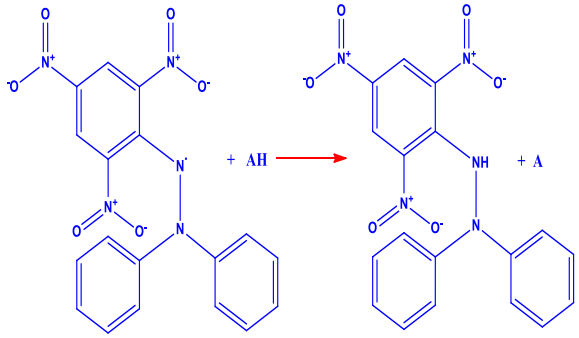

Figure 11: The reaction between the free radical DPPH and the antioxidant (AH) [39].

Nopitasari *et al.* evaluated the antioxidant activity of three complexes of organotin compounds, namely, complex (1): diphenyltin(IV) di-2-nitrobenzoate; complex (2): dibutyltin(IV) di-2-nitrobenzoate and complex (3): triphenyltin(IV) 2-nitrobenzoate by DPPH assay. All three complexes were studied by these techniques: UV, IR, and NMR. From the data on IC_{50}, complex (1) shows the highest antioxidant activity compared to complexes (2, 3). The inhibition percentage of the three complexes studied at different concentrations (2,4,8,16,32) µM is shown in Figure 12 [35].

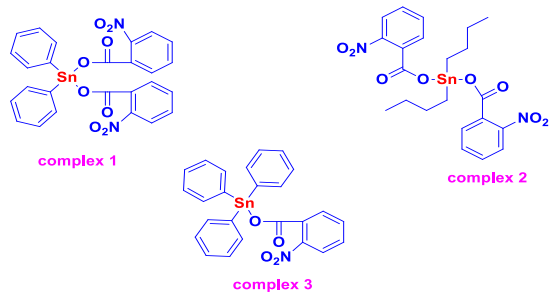

Figure 12: The structures of complex (1): diphenyltin(IV) di-2-nitrobenzoate, complex (2): dibutyltin(IV) di-2-nitrobenzoate and complex (3): triphenyltin(IV) 2-nitrobenzoate [40].

Also, Arraq *et al.* prepared three complexes by using the antibiotic cephalexin as a ligand. The three complexes are complex (1): Ph_2SnL_2, complex (2): Bu_2SnL_2, and complex (3): Me_2SnL_2. They were studied using ^1H, ^{13}C, and ^{119}Sn NMR, which shows that the geometries of the complexes are octahedral. All complexes were evaluated as antioxidants by DPPH and CUPRAC assays, which showed, based on the moiety of the organotin compound, that the three complexes [especially complex (3)] had higher antioxidant activity than cephalexin (ligand). The inhibition percentage of the three complexes at different times (5, 10, and 15 min) is shown in Figure 13 [40].

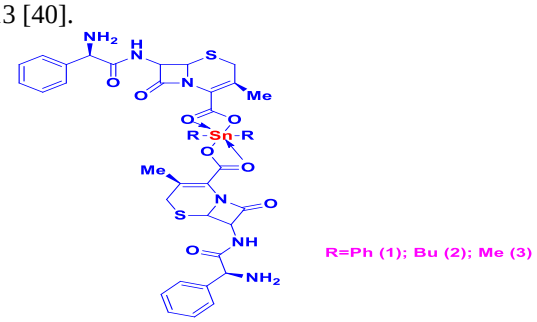

Figure 13: the structures of synthesized complex (1): Ph_2SnL_2, complex (2): Bu_2SnL_2 and complex (3): Me_2SnL_2 [41].

Another group of researchers prepared several complexes of organotin compounds, which are Bu_3SnL (1), Ph_3SnL (2), Me_2SnL_2 (3), and Bu_2SnL_2 (4), in the presence of para methoxy benzoic acid as a ligand, studied them by FTIR, ^1H and ^{119}Sn NMR, and evaluated them as antioxidants by the DPPH assay (Figure 14). Based on the moiety of tin metal, the results showed high antioxidant activity, especially for complex 3 [38].

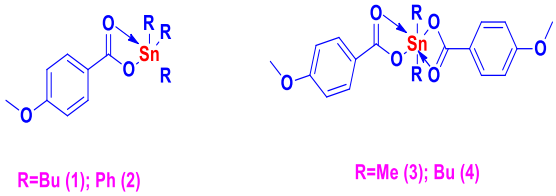

Figure 14: The structures of di and tri-organotin complexes which are Bu_3SnL (1), Ph_3SnL (2), Me_2SnL_2 (3) and Bu_2SnL_2 (4) in presence of Para Methoxy Benzoic Acid as ligand [38].

A large group of diorganotin(IV) complexes were prepared by Devi *et al*. (2019) R2SnL (R=Me, Et, Bu, and Ph) (Figure 15) by using different ligands and evaluated by usual techniques such as FT-IR, UV-Vis, and NMR. The results showed a dibasic tridentate ligand coordinated with tin metal. The complexes showed high free radical scavenging activity *in vitro* according to the DPPH assay, especially for complexes 16 and 20. The complexes showed high antioxidant activity because of the acidic nature of the hydrogen in the azomethine group and the negative charge of the benzene ring and other electrons in the withdrawing groups [41].

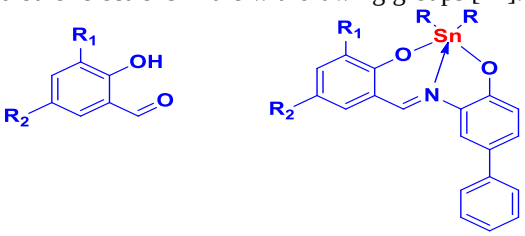

Figure 15: The structures of diorganotin(IV) complexes (5-20) (R=Me, Et, Bu and Ph) by using different ligands; 4-((2-hydroxybenzylidene) amino)-[1,1′-biphenyl]-3-ol (1), 4-((2-hydroxy-5-nitrobenzylidene)amino)- [1,1′-biphenyl]-3-ol (2), 4-((3-bromo-2-hydroxy-5-nitrobenzylidene)amino)- [1,1′-biphenyl]-3-ol (3) and 4-((3,5-dibromo-2-hydroxybenzylidene)amino)- [1,1′-biphenyl]-3-ol (4) [42].

Hashim *et al*. (2022) prepared four organotin(IV) complexes (Bu_2SnCl_2, Ph_2SnCl_2, Me_2SnCl_2, and Ph_3SnCl) from mefenamic acid as a ligand and tested them by the usual techniques (FTIR and NMR). They are evaluated for their antioxidant activity by DPPH assays, which demonstrate high antioxidant activity, and the dimethyl tin mefenamic acid complex showed the highest antioxidant activity (Figure 16), depending on the moiety of tin that raises the complex activity by improving the proton donor capacity of the ligand [42].

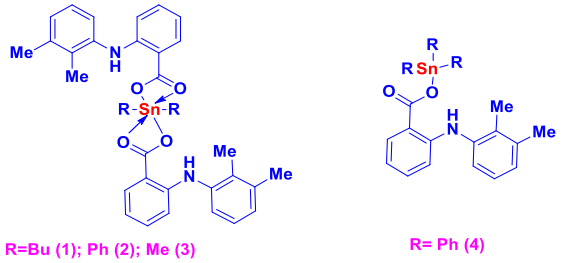

Figure 16: The structures of di and tri-organotin (IV) Complexes (Bu_2SnCl_2, Ph_2SnCl_2, Me_2SnCl_2, Ph_3SnCl) from Mefenamic acid as ligand [43].

Choudhary *et al*. (2019) synthesized two novel diorganotin complexes (Me_2SnL_2 and Bu_2SnL_2) from Me_2SnCl_2, n-Bu_2SnCl_2 and the ligand potassium 3,5-dinitrosalicylhydroxamate [3,5-$(NO_2)_2C_6H_2$(OH)CONHOK]; they were studied using IR, (^{1}H, ^{13}C,^{119}Sn) NMR, and mass spectrometry that showed five-coordinate distorted trigonal-bipyramidal geometry around the central metal. The synthesized complexes were evaluated as antioxidant agents and found to scavenge free radicals according to the DPPH assay. The results demonstrated the complexes' higher antioxidant activity than the ligand [43]. Sirajuddin *et al*. (2013) prepared a group of organotin(IV) complexes (R_2SnClL and R_3SnL) (Figure 17) and characterized them by FT-IR and (^{1}H, ^{13}C, and ^{119}Sn) NMR spectroscopy and their antioxidant properties were evaluated by DPPH assay; those results showed that the triorganotin(IV) complexes have higher antioxidant activity than diorganotin(IV) complexes based on their greater lipophilicity and cell membrane permeability [44].

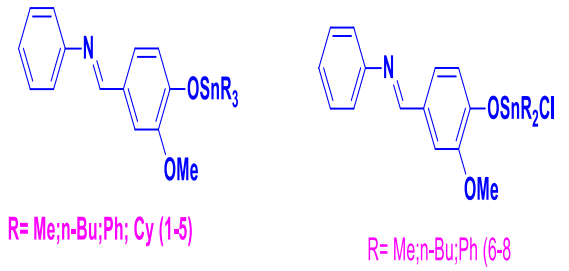

Figure 17. The organotin (IV) complexes (R_2SnClL and R_3SnL) where R = Me in complexes 1 and 6, n-Bu in complexes 2 and 7, Ph in complexes 3 and 8, tert-Bu in complex 4, Cy in complex 5 with 4-((3,5-dimethylphenylimino)methyl)-2- methoxyphenol) as ligand [45].

Conclusions

Organotin(IV) compounds are highly effective as anticancer and antioxidant agents. The anticancer activity was due to causing direct DNA damage via the increased Ca^{2+} concentration that leads to apoptosis. Organotin(IV) compounds act as antioxidants by decreasing the damaging effects of oxidants through their capacity to donate one electron to the oxidants, which inhibits their oxidative activity.

Conflicts of interest

There are no conflicts of interest.

Funding source

The authors did not receive any source of fund.

Data sharing statement

N/A

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