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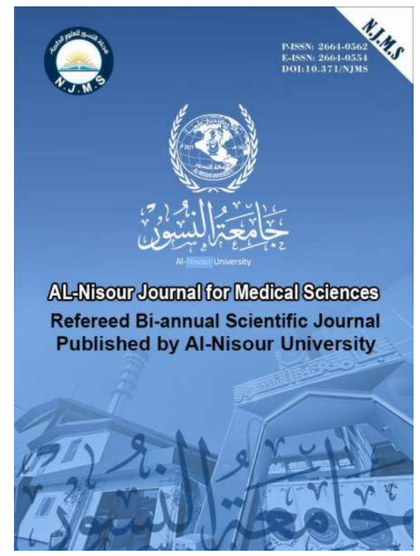

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Methyldopa: Chemistry, Structural Modifications, Pharmacological Activities, and Clinical Applications — A Comprehensive Review

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Abstract

Methyldopa (α-methyldopa) is a centrally acting antihypertensive drug that has been extensively prescribed for the management of hypertension, particularly in pregnant women, due to its established safety profile and non-teratogenic nature. Beyond its clinical use, methyldopa has attracted increasing scientific interest because of its unique chemical structure, which contains multiple oxygen- and nitrogen-donor functional groups capable of undergoing structural modification and metal coordination.

This comprehensive review highlights the chemical structure of methyldopa, its synthesis pathways, spectroscopic characteristics—particularly FTIR analysis—and its pharmacological mechanisms of action as an α_2-adrenergic receptor agonist. Special attention is given to methyldopa-induced adverse effects, including hepatotoxicity, immune-mediated reactions, and neuropsychiatric implications associated with hyperprolactinaemia.

Furthermore, recent advances in the utilization of methyldopa beyond conventional pharmacotherapy are discussed. These include its role as a functional monomer in molecularly imprinted polymers (MIPs) for highly selective electrochemical sensing applications, as well as its incorporation into metal and organotin(IV) complexes. Such complexes have demonstrated promising performance in diverse fields, including CO_2 storage, polymer photostabilization, and anticancer activity. Notably, methyldopa-derived triphenyltin complexes exhibit superior efficiency, attributed to enhanced aromatic interactions and improved physicochemical properties.

Overall, this review underscores the versatility of methyldopa as a multifunctional molecule bridging medicinal chemistry and materials science. The findings emphasize its potential for future development in advanced therapeutic systems, environmental applications, and functional materials, encouraging further interdisciplinary research on methyldopa-based derivatives and complexes.

Keywords: Methyldopa, Structural modifications, Pharmacological activities, Clinical applications, Antihypertensive agent

1. Introduction

Methyldopa is a well-known drug used mainly to treat high blood pressure and has been used in medical practice since the 1960s. It is marketed under the name Aldomet. The drug works by reducing the activity of the sympathetic nervous system, which helps lower blood pressure. This effect occurs because methyldopa stimulates presynaptic α2-adrenergic receptors, leading to a decrease in norepinephrine release from nerve endings.

Methyldopa is transported to the brain in a manner similar to amino acids and is then converted into its active form, methylnorepinephrine. During the production of neurotransmitters such as dopamine, norepinephrine, and epinephrine, methyldopa replaces DOPA, causing the formation of inactive neurotransmitters. As a result, nerve signals involved in blood pressure regulation are weakened, which contributes to its antihypertensive effect.

Clinically, methyldopa is commonly prescribed for patients with hypertension who also suffer from heart

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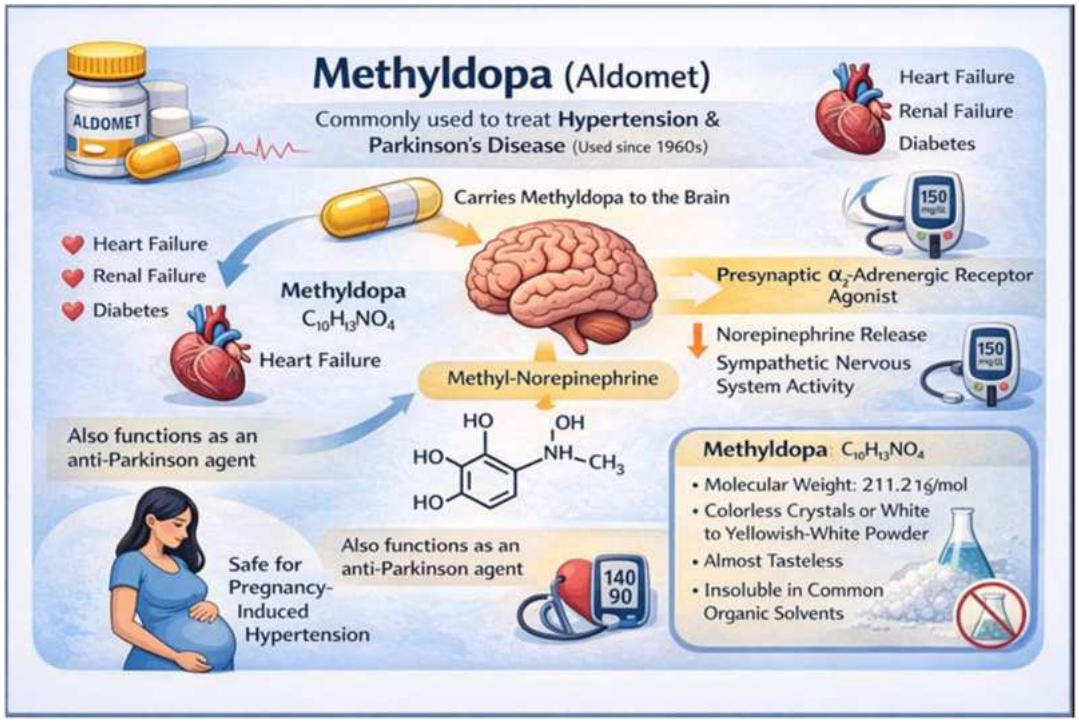


Fig. 1. Schematic representation of methyldopa showing its chemical structure, mechanism of action as a presynaptic α_2-adrenergic receptor agonist, and its clinical use in the treatment of hypertension, including pregnancy-induced hypertension.

disease, kidney disease, or diabetes. It is also considered a safe option for treating high blood pressure during pregnancy.

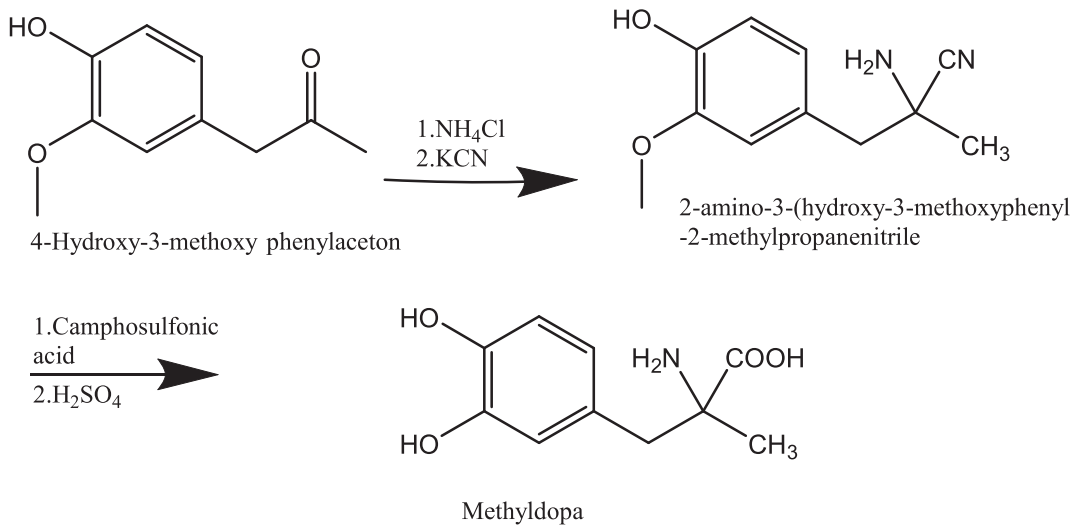
From a chemical perspective, methyldopa is a catecholamine derivative with the molecular formula $C_{10}H_{13}NO_4$ and a molecular weight of 211.21 g/mol. It appears as colorless to pale crystals or a white to slightly yellow powder, has almost no taste, and is poorly soluble in common organic solvents. The chemical structure of methyldopa is shown in Fig. 1.

Alpha-methyl-L-dopa is derived from L-tyrosine and contains a methyl group at the alpha position, along with an extra hydroxyl group at the 3-position of the phenyl ring. It functions as an antihypertensive drug by acting as an alpha-adrenergic agonist and reducing sympathetic nervous system activity. In addition, it exhibits sympatholytic properties and affects the peripheral nervous system. Structurally, it is classified as a non-proteinogenic L-alpha-amino acid related to L-tyrosine (PubChem).

1.1. Synthesis of methyldopa

The synthesis of methyldopa starts from 4-hydroxy-3-methoxy phenylacetone as the initial precursor, which undergoes reaction with ammonium chloride followed by potassium cyanide to form the corresponding α-aminonitrile intermediate. The L-isomer is then selectively separated via reaction with camphorsulfonic acid, and subsequent hydrolysis upon treatment with sulfuric acid affords methyldopa as the final product (PubChem), as illustrated in Scheme 1.

The FTIR spectrum of pure methyldopa exhibits several characteristic absorption bands corresponding to the functional groups present in the molecule. A broad and intense band appears in the region 3475–3200 cm^{-1}, which is attributed to overlapping O–H (phenolic and carboxylic) and N–H stretching vibrations. A sharp and well-defined peak is observed at ≈1715–1685 cm^{-1}, corresponding to the C=O stretching vibration of the carboxylic acid group, confirming the presence of a free and uncoordinated carboxyl functionality. Aromatic skeletal vibrations are clearly visible in the region 1600–1500 cm^{-1}, typically appearing near 1604–1510 cm^{-1}, which are characteristic of the benzene ring present in the structure. The C–O stretching bands of both the phenolic and carboxylic groups appear prominently between 1328–1220 cm^{-1}, while additional aromatic C–H in-plane and out-of-plane bending vibrations are observed within 1160–700 cm^{-1}, supporting the presence of a substituted catechol system (Silverstein *et al.*, 2005).



Scheme 1. Representation of the synthetic route for the preparation of methyldopa, illustrating the key reaction steps from starting materials to the final product.

1.2. Toxcicty of methyldopa

Liver injury caused by methyldopa was recognized soon after the drug was first introduced into clinical practice in the 1960s. Long-term use of methyldopa is commonly associated with mild and temporary increases in serum aminotransferase levels, which occur in about 5% to 35% of patients. In most cases, these enzyme elevations disappear even when treatment is continued.

However, serious or clinically evident liver damage due to methyldopa is relatively rare, although several hundred cases have been documented. Two main forms of methyldopa-related liver toxicity have been identified. The first is an acute hepatitis that develops within weeks to months after starting the drug. The second is a chronic hepatitis that appears after prolonged use, usually months to years following the initiation of therapy. These patterns of liver injury are illustrated in Fig. 2.

2. Mechanism of hepatotoxicity

Both the acute and chronic hepatic injury from methyldopa have features that suggest an immune etiology, although less allergic than autoimmune in character. These findings and metabolic studies suggest that methyldopa may induce an autoimmune liver injury (perhaps via a toxic metabolic intermediate serving as an antigenic hapten presented on the surface of hepatocytes) in susceptible hosts (Björnsson & Olsson, 2006).

2.1. Side effect of methyldopa

Common adverse effects include (Rang *et al.*, 2016):

- Nausea
- Diarrhea
- Headache
- Dizziness
- Sedation
- Dry mouth
- Rash

Rare yet clinically fatal adverse effects include (Wiciński *et al.*, 2020)

- Hemolytic anemia (Coombs positive)
- Lupus-like syndrome
- Myocarditis
- Pancreatitis
- Hepatotoxicity
- Immune thrombocytopenia
- Reversible leukopenia
- Involuntary choreoathetotic movements
- Weight gain (5)

2.2. Contraindication (Katzung & Trevor, 2021)

- Active hepatic disease
- Liver disorders due to previous therapy
- Direct Coombs positive hemolytic anemia
- Significant drug history of MAO inhibitor therapy
- Pheochromocytoma
- Known hypersensitivity to methyldopa in any form

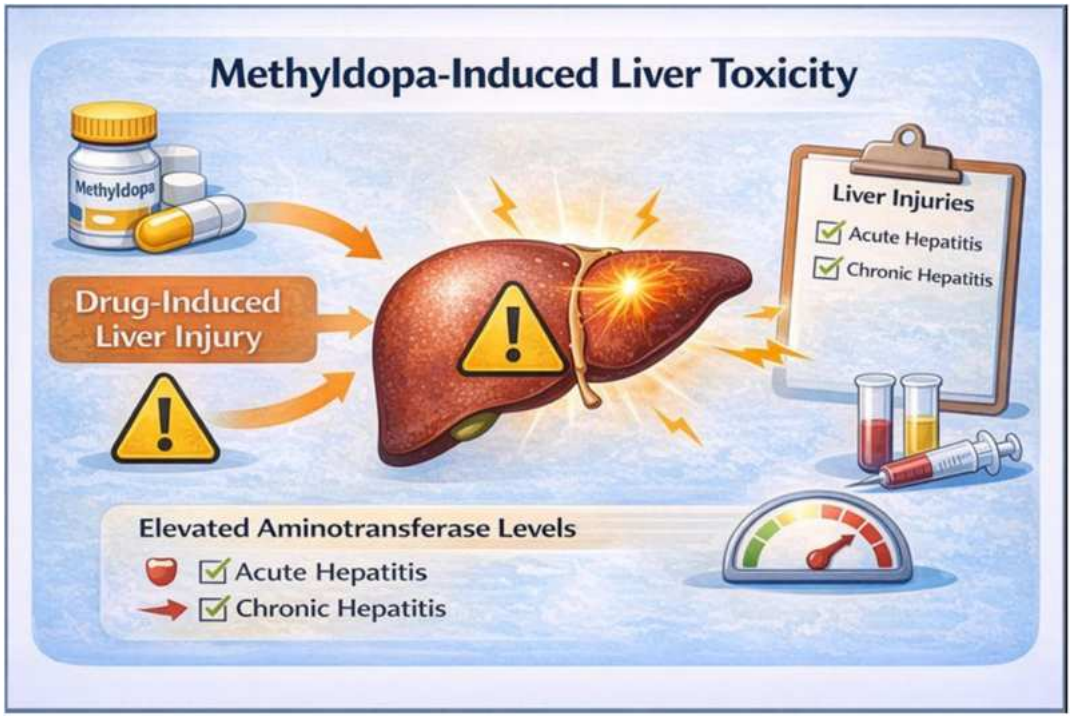


Fig. 2. Schematic illustration of methyldopa-induced liver toxicity, showing drug-related liver injury associated with elevated aminotransferase levels and the development of acute and chronic hepatitis during methyldopa therapy.

Fig. 3. Schematic representation of CO_2 storage in porous metal–Schiff base complexes, illustrating physical adsorption of CO_2 within micro- and mesopores, adsorption on internal pore surfaces, and weak interactions with metal active sites (Ni, Cu, and Co), highlighting their nano-sponge behavior and high surface area.

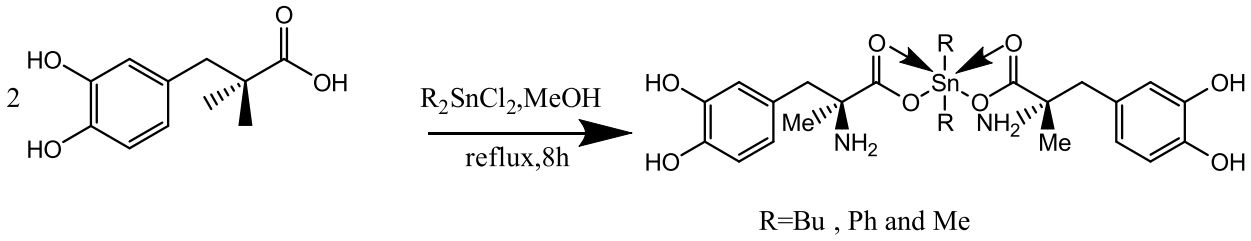
2.3. Methyldopa is used as a functional monomer to make imprinted nanopolymer nanoparticles

MIP-based sensor toward sofosbuvir. The presence of both phenolic and carboxylic functional groups in methyldopa facilitated strong and specific interactions with the template molecule, which explains the successful complex formation observed in the UV spectroscopic studies. These interactions played an essential role in generating well-defined recognition sites during the polymerization process.

The electropolymerization of methyldopa under optimized conditions resulted in the formation of a uniform poly(methyldopa) layer on the electrode surface. The optimization of parameters such as pH, number of polymerization cycles, potential window, and scan rate significantly enhanced the selectivity and sensitivity of the sensor. The surface and electrochemical characterization results confirmed not only the successful polymer deposition but also the creation of three-dimensional cavities complementary to sofosbuvir.

The high selectivity observed for the PMD–MIP sensor, even in the presence of high concentrations of interfering species, highlights the effectiveness of the molecular imprinting strategy. Moreover, the use of a ferrocyanide/ferricyanide redox probe enabled sensitive indirect detection. These findings demonstrate that the developed MIP sensor is a reliable and promising approach for the determination of sofosbuvir in complex matrices such as pharmaceutical formulations and human plasma (Yousif *et al.*, 2023).

Eamd and *et al.* in 2023 Carbon dioxide is stored inside the porous structure of the metal–Schiff base complexes. The storage does not occur in an external container; rather, the complexes themselves act as nano-sponge materials that capture CO_2 molecules. More specifically, CO_2 storage takes place mainly



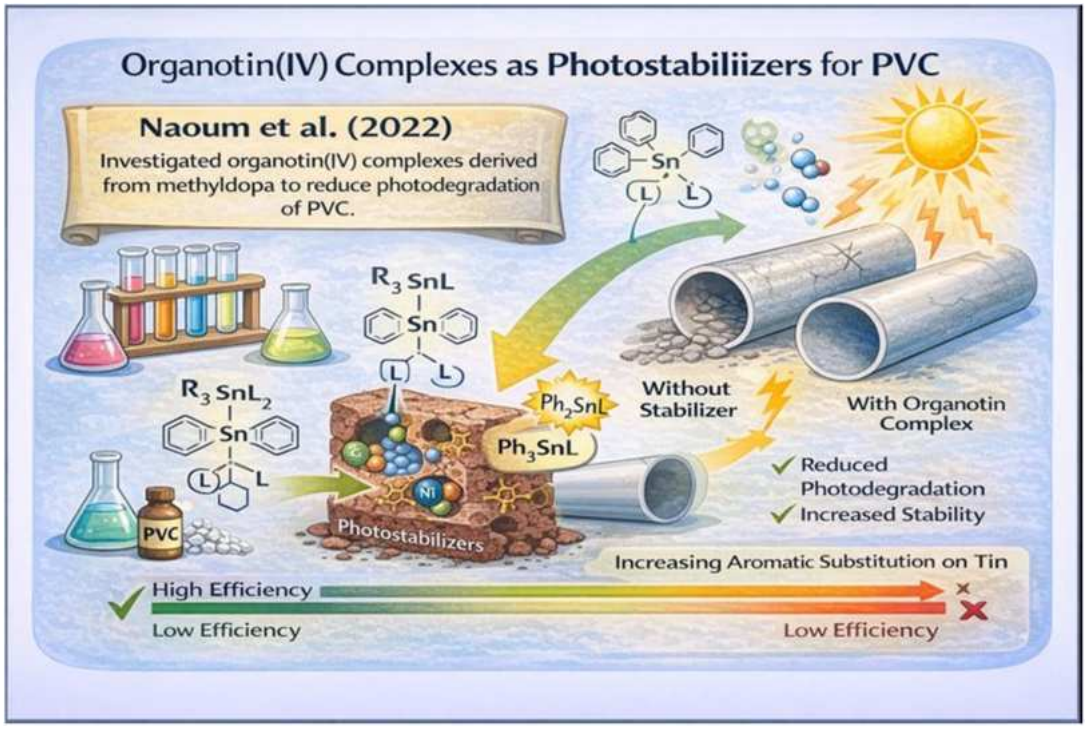


Fig. 4. Photostabilization of PVC by methyldopa-derived organotin(IV) complexes, highlighting the superior efficiency of the triphenyltin complex (Ph_3SnL) due to increased aromatic substitution on tin.

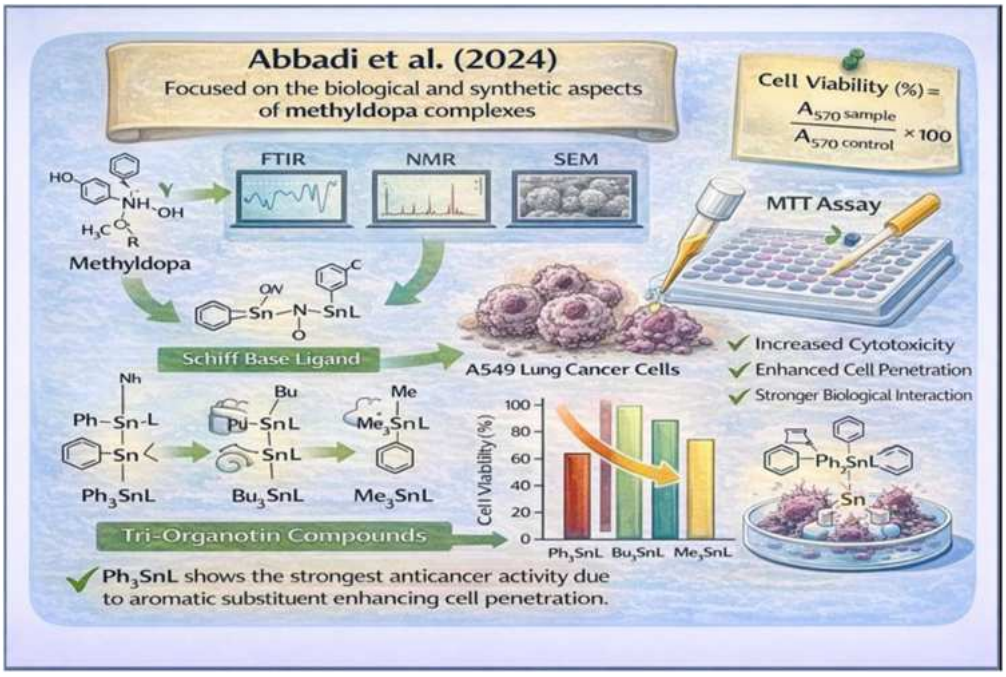
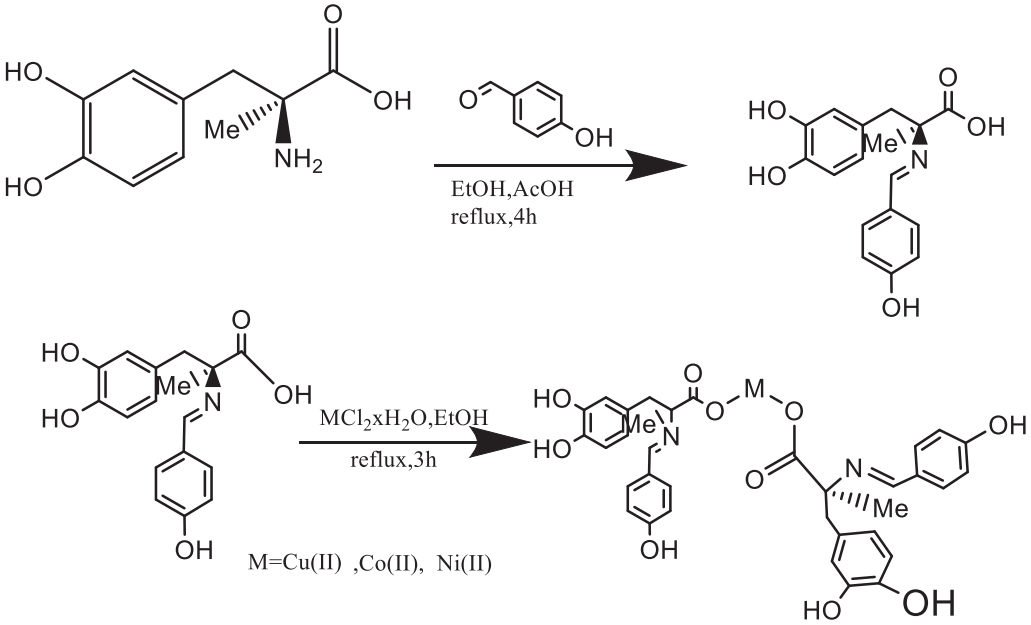


Fig. 5. Anticancer activity of methyldopa-derived tri-organotin complexes against A549 lung cancer cells, showing the highest cytotoxic effect for the Ph_3SnL complex as evaluated by the MTT assay.



Scheme 2. Photostabilization of PVC using methyldopa-derived organotin(IV) complexes, highlighting enhanced resistance to UV-induced degradation with the triphenyltin–methyldopa complex showing the highest efficiency.

within the internal pores (mesopores and icropores) of the complexes, where gas molecules enter and become physically adsorbed. In addition, part of the CO_2 is adsorbed onto the internal surface of the pores, while a smaller contribution arises from weak interactions between CO_2 molecules and the metal active sites (such as Ni, Cu, or Co), Fig. 3. The high surface area and porous nature of these complexes significantly enhance their CO_2 storage capacity, which is typically expressed as cm^3 of CO_2 per gram of material (Emad *et al.*, 2023).

Naoom *et al.* in 2022 investigated the effect of organotin(IV) complexes derived from methyldopa as photostabilizers for PVC. They synthesized

complexes of the types R_3SnL and R_2SnL_2, where the Ph_3SnL complex showed the highest efficiency in reducing photodegradation. Their results confirmed that increasing aromatic substitution on tin enhances the photostabilizing performance of the complexes (Naoom *et al.*, 2022) as shown below, Fig. 4.

Abbadi *et al.* in 2024 focused on the biological and synthetic aspects of methyldopa complexes. He first prepared a Schiff base ligand from methyldopa and then coordinated it with three tri-organotin compounds: Ph_3SnL, Bu_3SnL, and Me_3SnL. These complexes were characterized using FTIR, NMR, and SEM. He then evaluated their cytotoxic activity against A549 lung cancer cells using the MTT assay (Fig. 5) (Abbadi *et al.*, 2024), calculating cell viability using:

$$\text{Cell Viability (\%)} = \frac{A_{570\,\text{sample}}}{A_{570\,\text{control}}} \times 100$$

The findings demonstrated that Ph_3SnL showed the strongest anticancer activity, attributed to the aromatic substituent that enhances cellular penetration and biological interaction (Abbadi *et al.*, 2024), Fig. 5.

Imad *et al.* synthesized several methyldopa-based organotin(IV) complexes and investigated their application as photostabilizers for PVC. The complexes were characterized by FTIR and MR spectroscopy, confirming coordination through oxygen donor atoms. When incorporated nto PVC films, all complexes significantly enhanced resistance to UV-induced degradation, with the triphenyltin–methyldopa complex showing the highest efficiency. Photostability was evaluated using FTIR functional group indices, weight-loss measurements, and viscosity-average olecular weight calculations. The study demonstrated that methyldopa-derived organotin complexes are effective additives for improving PVC photostability (Imad *et al.*, 2023).

3. Conclusion

Methyldopa represents a well-established antihypertensive drug with a long clinical history, particularly in the management of hypertension during pregnancy, where its safety and non-teratogenic profile distinguish it from many other therapeutic agents. From a pharmacological perspective, its action as a centrally acting α_2-adrenergic receptor agonist effectively reduces sympathetic outflow, leading to sustained blood pressure control. However, long-term administration has been associated with several adverse effects, most notably hepatotoxicity, immune-mediated disorders, and neuropsychiatric manifestations linked to hyperprolactinaemia, highlighting the importance of careful clinical monitoring.

From a chemical standpoint, the molecular structure of methyldopa—characterized by phenolic hydroxyl groups, a carboxylic acid moiety, and an amino acid backbone—confers remarkable versatility. These functional groups enable diverse chemical transformations, including Schiff base formation and coordination with metal ions. Spectroscopic investigations, particularly FTIR analysis, confirm the integrity of these functional groups in the free drug and provide a reliable basis for tracking structural modifications upon derivatization or complexation.

Recent research has significantly expanded the scope of methyldopa beyond its traditional pharmaceutical role. Its application as a functional monomer in molecularly imprinted polymers has demonstrated high selectivity and sensitivity in electrochemical sensing platforms, reflecting its strong intermolecular interaction capabilities. Moreover, methyldopa-derived metal and organotin (IV) complexes have shown promising performance in materials science applications, including carbon dioxide storage and polymer photostabilization. The enhanced efficiency observed in aromatic organotin derivatives, particularly triphenyltin complexes, underscores the crucial role of structural features such as aromaticity and metal–ligand coordination in determining functional performance.

In addition, the biological evaluation of methyldopa-based organotin complexes has revealed noteworthy anticancer activity, with improved cytotoxic effects attributed to increased lipophilicity, cellular uptake, and synergistic interactions between the metal center and the ligand framework. These findings highlight the potential of methyldopa as a scaffold for designing multifunctional bioactive and industrial materials.

Overall, this review demonstrates that methyldopa is not merely a conventional antihypertensive drug, but a multifunctional molecule with broad interdisciplinary relevance. Its chemical adaptability and proven biological compatibility make it an attractive candidate for future research in medicinal chemistry, polymer science, environmental remediation, and metal-based therapeutics. Further studies focusing on structure–activity relationships, toxicity profiling, and long-term environmental impact are strongly recommended to fully exploit the potential of methyldopa-derived systems.

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by Nany Hairunisa

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Methyldopa: Chemistry, Structural Modifications, Pharmacological Activities, and Clinical Applications — A Comprehensive Review

Rania Kadhim [a], Emad Yousif [a,*], Suhad Ibrahim [a], Nany Hairunisa [b]

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[b] Occupational Medicine Department, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia

Abstract

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Furthermore, recent advances in the utilization of methyldopa beyond conventional pharmacotherapy are discussed. These include its role as a functional monomer in molecularly imprinted polymers (MIPs) for highly selective electrochemical sensing applications, as well as its incorporation into metal and organotin(IV) complexes. Such complexes have demonstrated promising performance in diverse fields, including CO_2 storage, polymer photostabilization, and anticancer activity. Notably, methyldopa-derived triphenyltin complexes exhibit superior efficiency, attributed to enhanced aromatic interactions and improved physicochemical properties.

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1. Introduction

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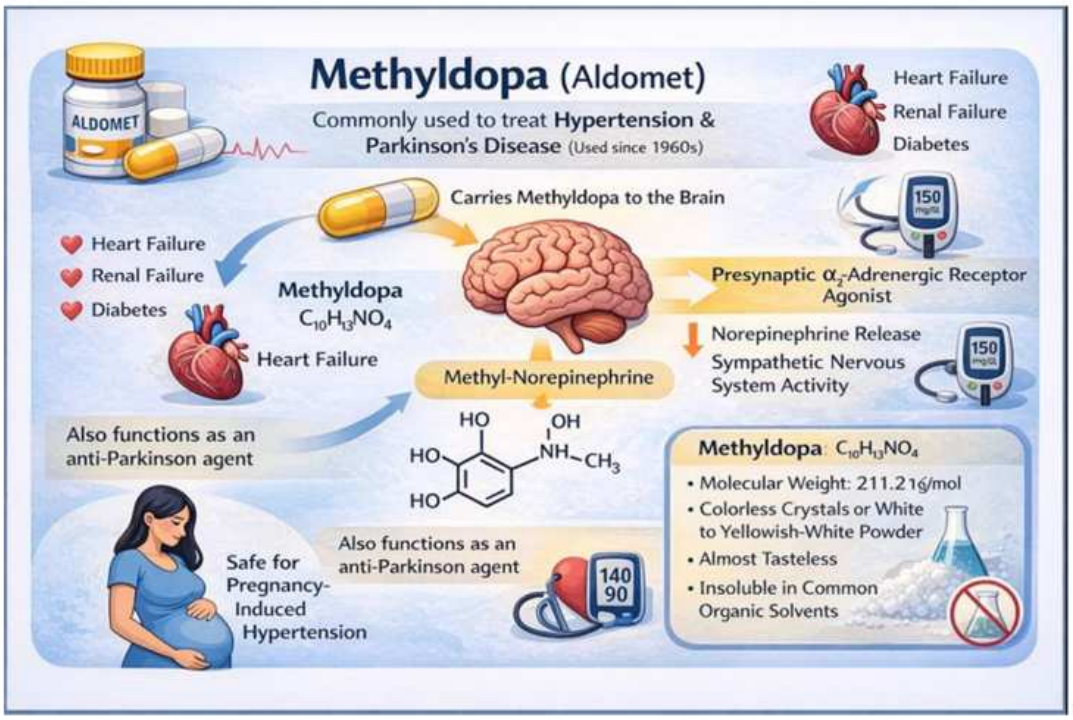

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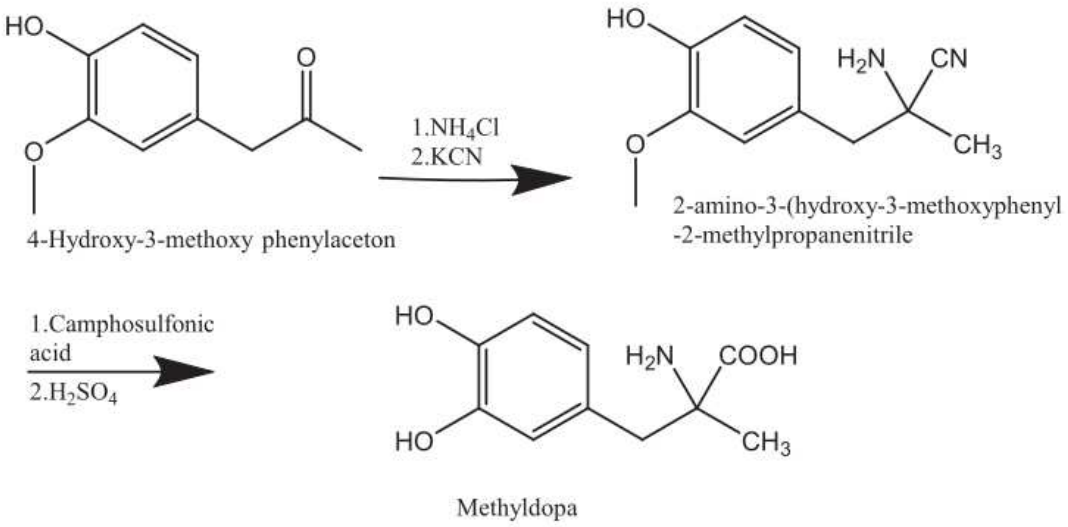
1.1. Synthesis of methyldopa

The synthesis of methyldopa starts from 4-hydroxy-3-methoxy phenylacetone as the initial precursor, which undergoes reaction with ammonium chloride followed by potassium cyanide to form the corresponding α-aminonitrile intermediate. The L-isomer is then selectively separated via reaction with camphorsulfonic acid, and subsequent hydrolysis upon treatment with sulfuric acid affords methyldopa as the final product (PubChem), as illustrated in Scheme 1.

The FTIR spectrum of pure methyldopa exhibits several characteristic absorption bands corresponding to the functional groups present in the molecule. A broad and intense band appears in the region 3475–3200 cm^{-1}, which is attributed to overlapping O–H (phenolic and carboxylic) and N–H stretching vibrations. A sharp and well-defined peak is observed at ≈1715–1685 cm^{-1}, corresponding to the C=O stretching vibration of the carboxylic acid group, confirming the presence of a free and uncoordinated carboxyl functionality. Aromatic skeletal vibrations are clearly visible in the region 1600–1500 cm^{-1}, typically appearing near 1604–1510 cm^{-1}, which are characteristic of the benzene ring present in the structure. The C–O stretching bands of both the phenolic and carboxylic groups appear prominently between 1328–1220 cm^{-1}, while additional aromatic C–H in-plane and out-of-plane bending vibrations are observed within 1160–700 cm^{-1}, supporting the presence of a substituted catechol system (Silverstein *et al.*, 2005).



Scheme 1. Representation of the synthetic route for the preparation of methyldopa, illustrating the key reaction steps from starting materials to the final product.

1.2. Toxcicty of methyldopa

Liver injury caused by methyldopa was recognized soon after the drug was first introduced into clinical practice in the 1960s. Long-term use of methyldopa is commonly associated with mild and temporary increases in serum aminotransferase levels, which occur in about 5% to 35% of patients. In most cases, these enzyme elevations disappear even when treatment is continued.

However, serious or clinically evident liver damage due to methyldopa is relatively rare, although several hundred cases have been documented. Two main forms of methyldopa-related liver toxicity have been identified. The first is an acute hepatitis that develops within weeks to months after starting the drug. The second is a chronic hepatitis that appears after prolonged use, usually months to years following the initiation of therapy. These patterns of liver injury are illustrated in Fig. 2.

2. Mechanism of hepatotoxicity

Both the acute and chronic hepatic injury from methyldopa have features that suggest an immune etiology, although less allergic than autoimmune in character. These findings and metabolic studies suggest that methyldopa may induce an autoimmune liver injury (perhaps via a toxic metabolic intermediate serving as an antigenic hapten presented on the surface of hepatocytes) in susceptible hosts (Björnsson & Olsson, 2006).

2.1. Side effect of methyldopa

Common adverse effects include (Rang *et al.*, 2016):

- Nausea
- Diarrhea
- Headache
- Dizziness
- Sedation
- Dry mouth
- Rash

Rare yet clinically fatal adverse effects include (Wiciński *et al.*, 2020)

- Hemolytic anemia (Coombs positive)
- Lupus-like syndrome
- Myocarditis
- Pancreatitis
- Hepatotoxicity
- Immune thrombocytopenia
- Reversible leukopenia
- Involuntary choreoathetotic movements
- Weight gain (5)

2.2. Contraindication (Katzung & Trevor, 2021)

- Active hepatic disease
- Liver disorders due to previous therapy
- Direct Coombs positive hemolytic anemia
- Significant drug history of MAO inhibitor therapy
- Pheochromocytoma
- Known hypersensitivity to methyldopa in any form

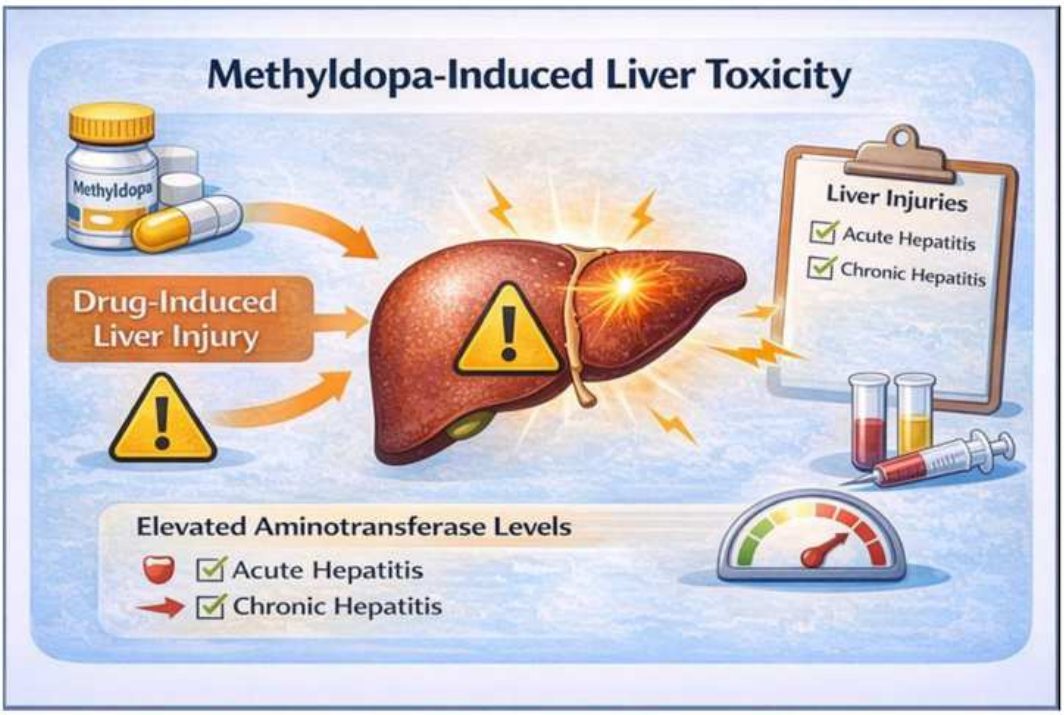


Fig. 2. Schematic illustration of methyldopa-induced liver toxicity, showing drug-related liver injury associated with elevated aminotransferase levels and the development of acute and chronic hepatitis during methyldopa therapy.

Fig. 3. Schematic representation of CO_2 storage in porous metal–Schiff base complexes, illustrating physical adsorption of CO_2 within micro- and mesopores, adsorption on internal pore surfaces, and weak interactions with metal active sites (Ni, Cu, and Co), highlighting their nano-sponge behavior and high surface area.

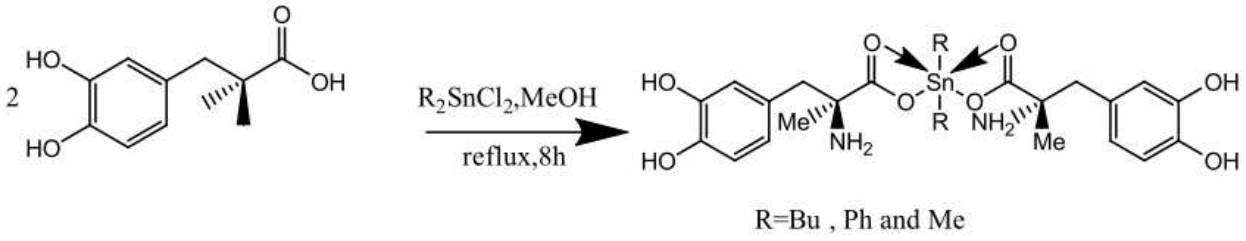
2.3. Methyldopa is used as a functional monomer to make imprinted nanopolymer nanoparticles

MIP-based sensor toward sofosbuvir. The presence of both phenolic and carboxylic functional groups in methyldopa facilitated strong and specific interactions with the template molecule, which explains the successful complex formation observed in the UV spectroscopic studies. These interactions played an essential role in generating well-defined recognition sites during the polymerization process.

The electropolymerization of methyldopa under optimized conditions resulted in the formation of a uniform poly(methyldopa) layer on the electrode surface. The optimization of parameters such as pH, number of polymerization cycles, potential window, and scan rate significantly enhanced the selectivity and sensitivity of the sensor. The surface and electrochemical characterization results confirmed not only the successful polymer deposition but also the creation of three-dimensional cavities complementary to sofosbuvir.

The high selectivity observed for the PMD–MIP sensor, even in the presence of high concentrations of interfering species, highlights the effectiveness of the molecular imprinting strategy. Moreover, the use of a ferrocyanide/ferricyanide redox probe enabled sensitive indirect detection. These findings demonstrate that the developed MIP sensor is a reliable and promising approach for the determination of sofosbuvir in complex matrices such as pharmaceutical formulations and human plasma (Yousif *et al.*, 2023).

Eamd and *et al.* in 2023 Carbon dioxide is stored inside the porous structure of the metal–Schiff base complexes. The storage does not occur in an external container; rather, the complexes themselves act as nano-sponge materials that capture CO_2 molecules. More specifically, CO_2 storage takes place mainly



R=Bu , Ph and Me

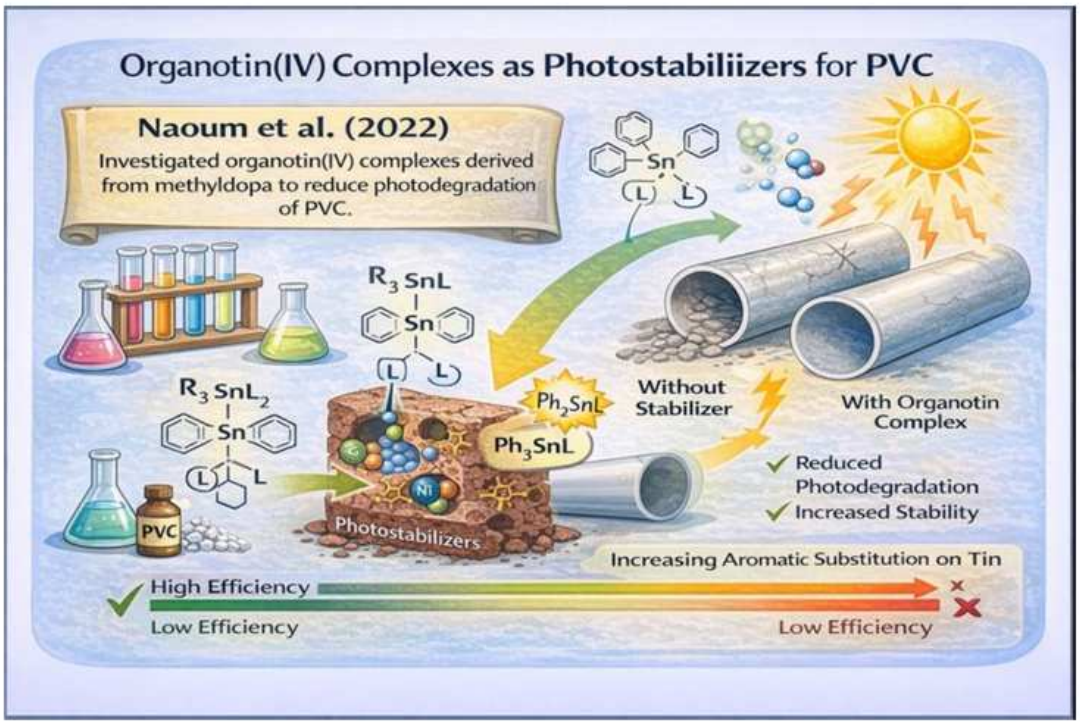


Fig. 4. Photostabilization of PVC by methyldopa-derived organotin(IV) complexes, highlighting the superior efficiency of the triphenyltin complex (Ph_3SnL) due to increased aromatic substitution on tin.

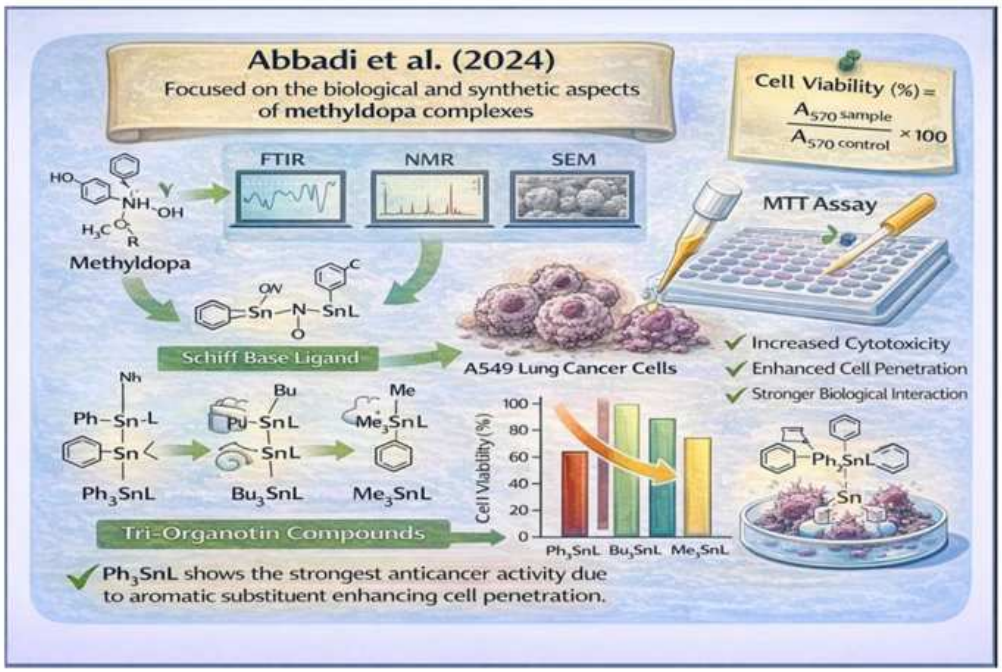
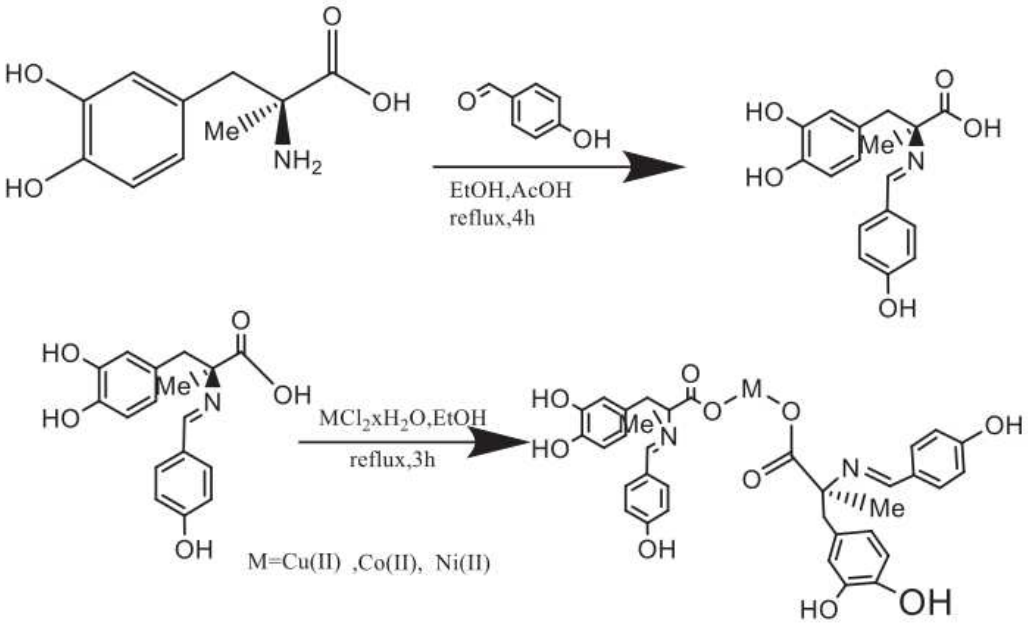


Fig. 5. Anticancer activity of methyldopa-derived tri-organotin complexes against A549 lung cancer cells, showing the highest cytotoxic effect for the Ph_3SnL complex as evaluated by the MTT assay.



Scheme 2. Photostabilization of PVC using methyldopa-derived organotin(IV) complexes, highlighting enhanced resistance to UV-induced degradation with the triphenyltin–methyldopa complex showing the highest efficiency.

within the internal pores (mesopores and icropores) of the complexes, where gas molecules enter and become physically adsorbed. In addition, part of the CO_2 is adsorbed onto the internal surface of the pores, while a smaller contribution arises from weak interactions between CO_2 molecules and the metal active sites (such as Ni, Cu, or Co), Fig. 3. The high surface area and porous nature of these complexes significantly enhance their CO_2 storage capacity, which is typically expressed as cm^3 of CO_2 per gram of material (Emad *et al.*, 2023).

Naoom *et al.* in 2022 investigated the effect of organotin(IV) complexes derived from methyldopa as photostabilizers for PVC. They synthesized

complexes of the types R_3SnL and R_2SnL_2, where the Ph_3SnL complex showed the highest efficiency in reducing photodegradation. Their results confirmed that increasing aromatic substitution on tin enhances the photostabilizing performance of the complexes (Naoom *et al.*, 2022) as shown below, Fig. 4.

Abbadi *et al.* in 2024 focused on the biological and synthetic aspects of methyldopa complexes. He first prepared a Schiff base ligand from methyldopa and then coordinated it with three tri-organotin compounds: Ph_3SnL, Bu_3SnL, and Me_3SnL. These complexes were characterized using FTIR, NMR, and SEM. He then evaluated their cytotoxic activity against A549 lung cancer cells using the MTT assay (Fig. 5) (Abbadi *et al.*, 2024), calculating cell viability using:

$$\text{Cell Viability (\%)} = \frac{A_{570\,\text{sample}}}{A_{570\,\text{control}}} \times 100$$

The findings demonstrated that Ph_3SnL showed the strongest anticancer activity, attributed to the aromatic substituent that enhances cellular penetration and biological interaction (Abbadi *et al.*, 2024), Fig. 5.

Imad *et al.* synthesized several methyldopa-based organotin(IV) complexes and investigated their application as photostabilizers for PVC. The complexes were characterized by FTIR and MR spectroscopy, confirming coordination through oxygen donor atoms. When incorporated nto PVC films, all complexes significantly enhanced resistance to UV-induced degradation, with the triphenyltin–methyldopa complex showing the highest efficiency. Photostability was evaluated using FTIR functional group indices, weight-loss measurements, and viscosity-average olecular weight calculations. The study demonstrated that methyldopa-derived organotin complexes are effective additives for improving PVC photostability (Imad *et al.*, 2023).

3. Conclusion

Methyldopa represents a well-established antihypertensive drug with a long clinical history, particularly in the management of hypertension during pregnancy, where its safety and non-teratogenic profile distinguish it from many other therapeutic agents. From a pharmacological perspective, its action as a centrally acting α_2-adrenergic receptor agonist effectively reduces sympathetic outflow, leading to sustained blood pressure control. However, long-term administration has been associated with several adverse effects, most notably hepatotoxicity, immune-mediated disorders, and neuropsychiatric manifestations linked to hyperprolactinaemia, highlighting the importance of careful clinical monitoring.

From a chemical standpoint, the molecular structure of methyldopa—characterized by phenolic hydroxyl groups, a carboxylic acid moiety, and an amino acid backbone—confers remarkable versatility. These functional groups enable diverse chemical transformations, including Schiff base formation and coordination with metal ions. Spectroscopic investigations, particularly FTIR analysis, confirm the integrity of these functional groups in the free drug and provide a reliable basis for tracking structural modifications upon derivatization or complexation.

Recent research has significantly expanded the scope of methyldopa beyond its traditional pharmaceutical role. Its application as a functional monomer in molecularly imprinted polymers has demonstrated high selectivity and sensitivity in electrochemical sensing platforms, reflecting its strong intermolecular interaction capabilities. Moreover, methyldopa-derived metal and organotin (IV) complexes have shown promising performance in materials science applications, including carbon dioxide storage and polymer photostabilization. The enhanced efficiency observed in aromatic organotin derivatives, particularly triphenyltin complexes, underscores the crucial role of structural features such as aromaticity and metal–ligand coordination in determining functional performance.

In addition, the biological evaluation of methyldopa-based organotin complexes has revealed noteworthy anticancer activity, with improved cytotoxic effects attributed to increased lipophilicity, cellular uptake, and synergistic interactions between the metal center and the ligand framework. These findings highlight the potential of methyldopa as a scaffold for designing multifunctional bioactive and industrial materials.

Overall, this review demonstrates that methyldopa is not merely a conventional antihypertensive drug, but a multifunctional molecule with broad interdisciplinary relevance. Its chemical adaptability and proven biological compatibility make it an attractive candidate for future research in medicinal chemistry, polymer science, environmental remediation, and metal-based therapeutics. Further studies focusing on structure–activity relationships, toxicity profiling, and long-term environmental impact are strongly recommended to fully exploit the potential of methyldopa-derived systems.

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