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A Comprehensive Review of the Synthesis, Characterization, and Therapeutic Potential of Gold, Platinum, and Ruthenium Complexes and Organic Compounds

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Review

A Comprehensive Review of the Synthesis, Characterization, and Therapeutic Potential of Gold, Platinum, and Ruthenium Complexes and Organic Compounds

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Abstract

The synthesis and systematic investigation of inorganic and organic compounds represent a crucial area in medicinal and pharmaceutical chemistry, particularly in the pursuit of novel therapeutic agents. This study reports on the preparation, structural analysis, and evaluation of selected inorganic and organic compounds with emphasis on their physicochemical characteristics and biological activities. Both categories of compounds were examined for their potential therapeutic relevance, including anticancer, antimicrobial, and anti-inflammatory properties. Inorganic complexes, particularly those incorporating transition metals, demonstrated promising activity that may be attributed to their ability to interact with bimolecular targets and modulate cellular pathways. Similarly, organic derivatives revealed bioactive features that merit further exploration. Collectively, the results underscore the therapeutic potential of synthesized compounds and contribute to the growing field of drug design involving both inorganic and organic frameworks. This work emphasizes the integration of synthetic chemistry, as well as natural products with biological evaluation as a pathway toward identifying effective molecules with clinical relevance. In this review, we highlight recently developed Au(I/III), Pt(II/IV), and Ru(II/III) complexes that have demonstrated notable in vivo anticancer activity between 2016 and 2025, along with the antimicrobial and anti-inflammatory properties of various inorganic and organic compounds. Our review emphasizes on gold, platinum and ruthenium complexes synthesis and characterizations of inorganic and organic compounds with biomedical potential. The main focus is on the antitumor effects reported in 89 articles of inorganic and organic compounds, 53 on antimicrobial action and 17 on anti-inflammatory activities. In our review we cover the synthesis (30 articles) and characterizations (30 papers) of inorganic and organic compounds with potential biological and therapeutic effects. It is anticipated that this review will serve as a valuable resource in the future, particularly for professionals engaged in clinical, medical, and health-related disciplines.

Keywords: inorganic compounds; organic compounds; metallodrugs; anticancer; antimicrobial; anti-inflammatory properties; gold(I/III)-based anti-cancer compounds; platinum(II/IV)-based anti-cancer compounds; ruthenium(II/III)-based anti-cancer compounds

1. Introduction

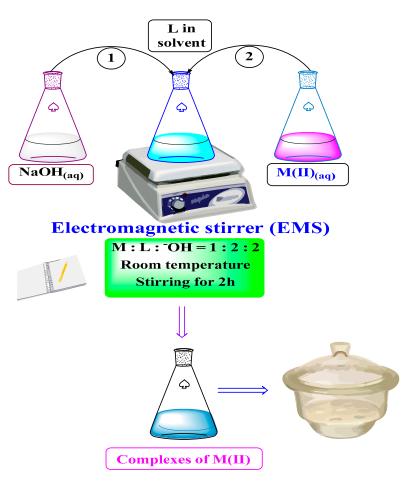
In recent years, cancer has been a scourge of modern society that is global and widespread. Oncogenes is may occur through the synergistic influence of two principal classes of exogenous agents: chemical carcinogens (including asbestos, tobacco-derived polycyclic aromatic hydrocarbons,

aflatoxins, and arsenic compounds), physical carcinogens (notably ultraviolet radiation and ionizing radiation), and endogenous genetic susceptibilities arising from individual hereditary backgrounds. Metal-based therapeutic and diagnostic agents occupy a crucial position in modern medicine due to their widespread application in the treatment and detection of diverse pathological conditions. Many metallopharmaceuticals are currently being evaluated in clinical trials, highlighting the therapeutic potential of metal-containing compounds in disease treatment. The core mechanisms responsible for the bioactivity of metallodrugs and imaging agents are now well understood.

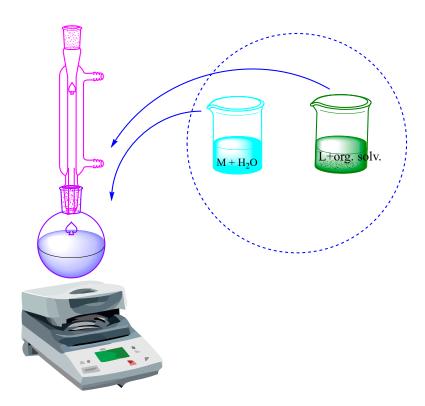
This review will focus on the use and potential of metal complexes and the biological activity of organic compounds as important therapeutic agents for the treatment of cancer. Our review provides a more focused, updated, and detailed perspective on the synthesis and characterizations of inorganic and organic compounds with biological effect, especially antitumor, antibacterial and anti-inflammatory activities. Unlike other reviews, we include not only metal complexes with potential therapeutic properties, but also organic compounds and natural products with anticancer, anti-inflammatory and antibacterial effects. We hope this review will be useful in the future especially for people who work in the areas of clinical, medical and other health applications.

1.1. The Synthesis of Metal Complexes

The preparation of coordination complexes has advanced remarkably, utilizing both traditional and contemporary methodologies to enhance their efficiency, durability, and performance (refer to Schemes 1 and 2). Analytical approaches, including spectroscopic, crystallographic, and electrochemical techniques, are essential for elucidating their structural details and directing their practical use.



Scheme 1. Preparation of coordination compounds at ambient temperature.



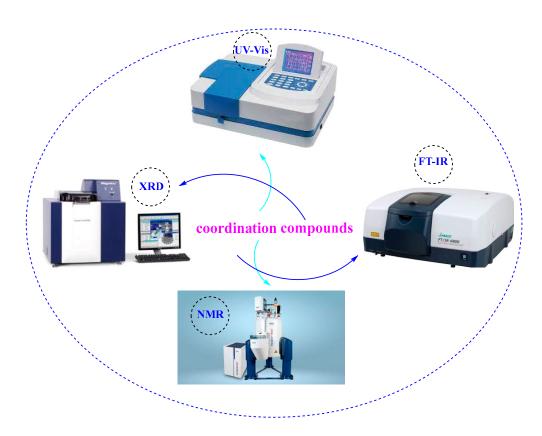
Scheme 2. Synthesis of complexes under heating conditions.

So far, a wide range of metal complexes with various organic ligands have been synthesized according to Scheme 1 at ambient temperature [1–17] or Scheme 2 under heating conditions [18–30].

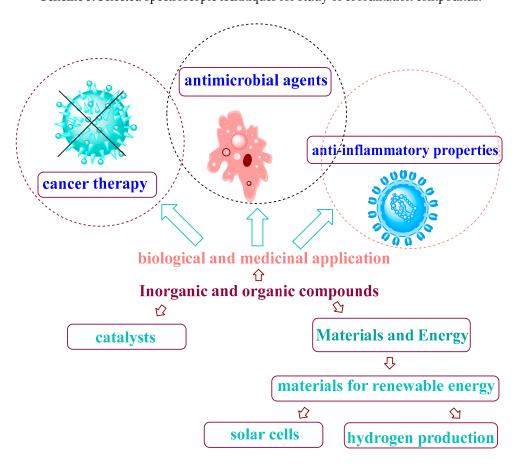
1.2. Analytical Approaches, Including Spectroscopic, Crystallographic, and Electrochemical Techniques for Characterization of Coordination Compounds

The characterization of metal complexes involves examining their chemical composition, structural attributes, and electronic properties to better understand their reactivity, functionality, and potential applications (see Schemes 3 and 4). A variety of analytical and spectroscopic techniques are employed for this purpose. X-ray crystallography [4,8–10,12,13,17,23–27,31–40] serves as a cornerstone for elucidating the three-dimensional atomic arrangement, yielding accurate geometrical information about the coordination environment. The molecular structures of some copper complexes are presented in Figure 1 and Figure 2, respectively [9,27]. UV–Vis spectroscopy [6,12,41–45] provides valuable information on electronic transitions in metal–ligand systems, thereby shedding light on ligand-field effects and electronic structures. Infrared (IR) spectroscopy is instrumental in identifying functional groups and vibrational modes, clarifying ligand types and binding patterns [4,7,10,12,13,46–52]. Moreover, NMR spectroscopy—in either solution or solid state [7,12,53–60]—offers detailed information on the nuclear environments within ligands, particularly in diamagnetic complexes.

Cheng and colleagues emphasized the catalytic role of the cobalt complex they obtained with 4′-pyridyl: 2,2′;6′,2″-terpyridine [10], as well as the anticancer activities of a dinuclear Fe(III) complex [10]. Lavrenova and co-worker synthesized novel complex of copper(II) with 2,5-bis(ethylthio)-1,3,4-thiadiazole with compositions $Cu(L^1)_2Br_2$ [27]. The metal Cu^{2+} ion was coordinated by two nitrogen atoms from monodentate ligands along with two bromide ions, forming a { CuN_2Br_2 } coordination polyhedron [27]. Figure 1 illustrates the molecular structure of the copper(II) complex.



Scheme 3. Selected spectroscopic techniques for study of coordination compounds.



Scheme 4. Inorganic and organic compounds including their potential therapeutic and other applications.

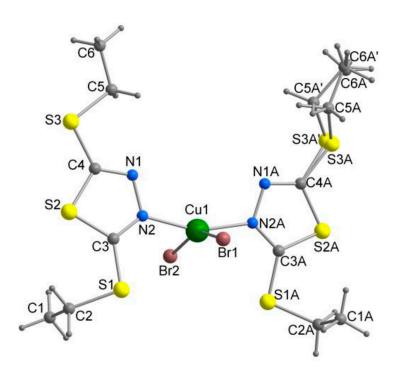


Figure 1. Structure of the molecule of copper(II) complex [27].

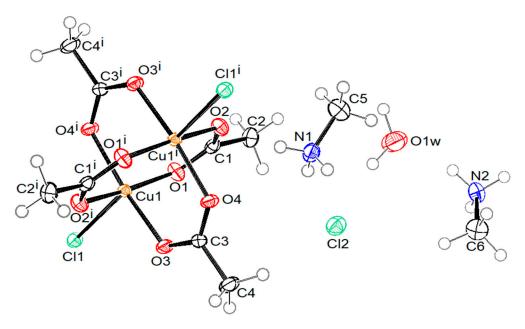


Figure 2. ORTEP drawing of copper complex with labelling of non-H atoms. Ellipsoids are drawn at 50% level. (i: x + 1, -y, -z + 1.) [9].

Recently, Golobič et al. reported the successful synthesis of new copper(II) complexes containing acetato and chlorido ligands with methylammonium as the counterion [9]. The structures of these complexes were determined by X-ray crystallography (see Figure 2). The analysis revealed a dinuclear coordination anion, $[Cu_2(Ac)_4Cl_2]^{2-}$, featuring bridging acetato ligands in a paddle-wheel arrangement and square-pyramidal coordination geometry around the Cu(II) centers [9].

This paper aims to summarize recent advances in the synthesis, characterization, and anticancer, antimicrobial and anti-inflammatory evaluation of inorganic and organic compounds, emphasizing gold(I/III), platinum(II/IV), ruthenium(II/III)-based anti-cancer compounds, to highlight their therapeutic potential and guide future design of more effective and selective anticancer agents useful for clinical, medical and health applications.

1.3. Biological and Medicinal Application of Inorganic Compounds

Gold(I/III)-Based Anti-Cancer Compounds

The medicinal use of gold dates back to antiquity, with Au(I) and Au(III) identified as the therapeutically active oxidation states. These gold-based compounds exhibit excellent biocompatibility and possess a broad spectrum of pharmacological activities, including anticancer, anti-inflammatory, and antirheumatic properties [61,62]. Gold-based complexes, particularly those containing carbene, phosphine, porphyrin, or dithiocarbamate ligands, act via mechanisms such as DNA disruption, apoptosis induction, and angiogenesis inhibition. Gold nanoparticles can also serve as targeted delivery systems, minimizing harm to healthy tissues [63]. Advances in Au(I)–N-heterocyclic carbene structures and other noble metal complexes highlight their promise as selective anticancer agents [64,65]. Figure 3 depicts representative Au(I) and Au(III) complexes investigated for anticancer activity.

Figure 3. Au(I) and (III) complexes, reported in the literature for their effects as possible anticancer drugs [65].

Gold(I) phosphine complexes showed strong cytotoxic effect against colon, lung, and ovarian cancer cells, with IC $_{50}$ values comparable to or surpassing cisplatin [66]. Four novel mononuclear gold(I) complexes also exhibited potent effects against HeLa, PC-3, A549, and HT-1080 cell lines, with one complex displaying IC $_{50}$ values as low as 0.08 μ M [67]. Their anticancer mechanism involves inhibition of TrxR and disruption of ATP levels, ultimately leading to cell death [65] (see Figure 4).

In 1985, Mirabelli et al. highlighted the anticancer potential of auranofin, a gold(I) complex, opening new avenues in gold-based chemotherapy [68]. Subsequent developments include doxorubicin-loaded, PEG-functionalized gold nanoparticles, which have shown selective cytotoxicity in cancer cells in vitro and in vivo [69]. Despite persistent challenges such as poor solubility, the emergence of drug resistance and systemic toxicity, ongoing research continues to focus on enhancing the pharmacokinetic properties and minimizing the adverse effects of gold-based therapeutics. Among these, gold(I) phosphane and azolate/phosphane complexes have exhibited remarkable cytotoxicity, including efficacy against chemoresistant cancer cell lines [70,71], underscoring their promise as selective anticancer agents. Carbene-derived gold(I) complexes, such as Au-1 and 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl-1-thiolate, have demonstrated potent

antiproliferative effects both in vitro and in vivo, with Au-1 notably reducing Ki67 expression, thereby highlighting its significant anticancer potential [72]. Representative examples of the anticancer activities of gold complexes are summarized in Table 1. Gold(III)-N-heterocyclic carbene complexes, exemplified by Au-3 synthesized via radioactive 12 d2 labeling, have facilitated in vivo imaging and exhibited low-micromolar IC₅₀ values, emphasizing the critical role of Au(III) to Au(I) reduction in achieving therapeutic efficacy [73]. Furthermore, structural modifications in phosphine ligands have been shown to markedly influence biological activity. Both auranofin and newly developed gold complexes effectively inhibited multiple myeloma tumor progression and induced apoptotic cell death [74]. The square-planar Au(III) complex Au-5 showed high selectivity toward malignant cells, with significantly reduced toxicity to normal cells and IC₅₀ values ranging from 20 to 34 µg/mL, suggesting superior tumor-targeting potential relative to cisplatin [75]. Schiff base ligands, recognized for their chelating versatility and pharmacological activity, have been widely applied in Au(III) coordination chemistry. Several Schiff base-derived Au(III) complexes exhibited cytotoxicity against hepatocellular carcinoma models, coordinating via azomethine nitrogen and phenolic oxygen in square-planar geometries. Mirzadeh et al. introduced mixed-valent Au(I)-Au(III) dinuclear complexes that selectively inhibit thioredoxin reductase, with confirmed physiological stability [76]. Notably, Au-6 displayed enhanced hydrophilicity, while chiral Au(III) complexes such as Au-7 demonstrated potent cytotoxicity (IC₅₀ = $1.3-2.95 \mu M$), induced ROS generation, mitochondrial dysfunction, and apoptosis in aggressive cancer cell lines, and modestly reduced tumor growth in vivo, highlighting their therapeutic potential [77].

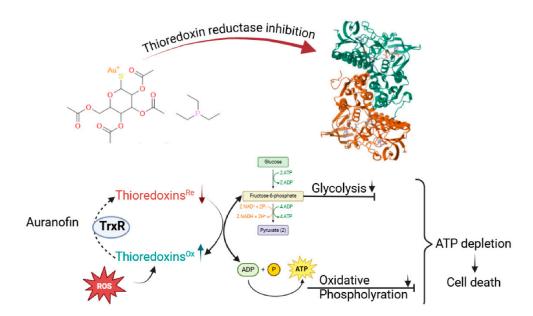
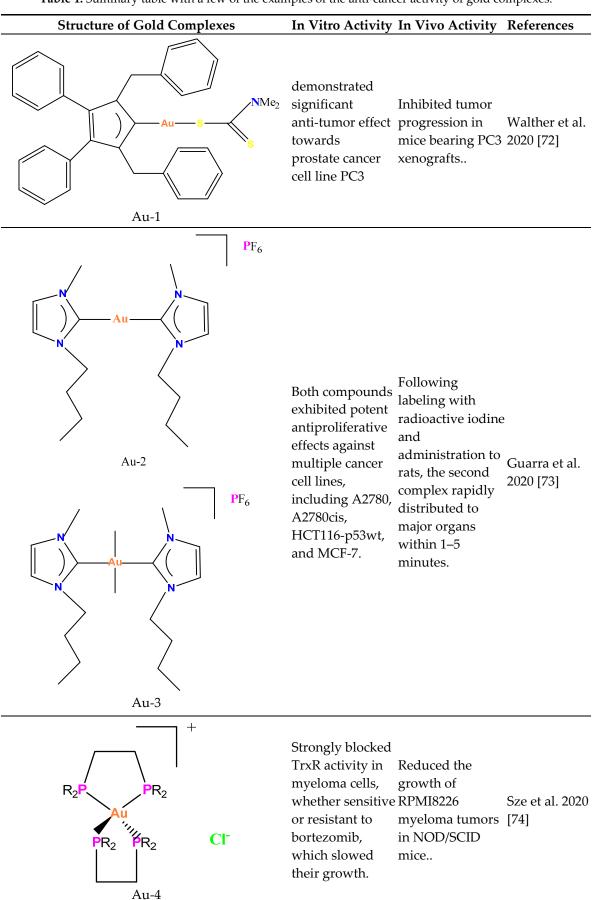


Figure 4. Mechanism of action of auranofin and gold complexes by interfering with TrxR and destabilizing ATP levels, causing cell death [65].

Table 1. Summary table with a few of the examples of the anti-cancer activity of gold complexes.



Recent investigations have underscored the anticancer potential of diverse gold-based complexes. Kumar et al. reported that Au(I) complexes incorporating thiolate, dithiocarbamate, and Schiff base ligands display pronounced cytotoxicity across multiple cancer cell lines [78]. Checconi et al. reported new Au(I) complexes with anticancer and antiviral activity [79]. Marinova et al. synthesized Cu(II), Pd(II), and Au(III) complexes with 2-thiouracil and related derivatives, evaluating their biological activity [80–83]. Comprehensive reviews by Komeda et al. and Todorov et al. discussed platinum-based drugs, such as cisplatin, and alternative metal complexes—including gold, ruthenium, lanthanum, and gallium—emphasizing their mechanisms and therapeutic potential

Au-7

[84,85]. Wang et al. identified an all-Au(I) phosphine complex with potent cytotoxicity against prostate cancer cells, surpassing the antitumor effects of cisplatin and auranofin [86].

Platinum-Based Anti-Cancer Compounds

Platinum-based chemotherapeutics continue to play a pivotal role in medicinal inorganic chemistry, with ongoing efforts aimed at enhancing cytotoxicity, improving selectivity, and minimizing systemic toxicity. To this end, novel mononuclear Pt(II) complexes featuring diverse ligands have been developed to augment anticancer efficacy across various tumor models. Cisdiamminedichloroplatinum (cisplatin), first synthesized in 1844 by Michele Peyrone, exhibited remarkable biological activity when its properties were identified by Barnett Rosenberg in 1965. Following initial bacterial assays, cisplatin progressed to clinical trials in 1971 and received FDA approval in 1978, establishing a foundation for modern platinum-based chemotherapy [87–91]. Figure 5 illustrates platinum drugs currently in clinical use [91].

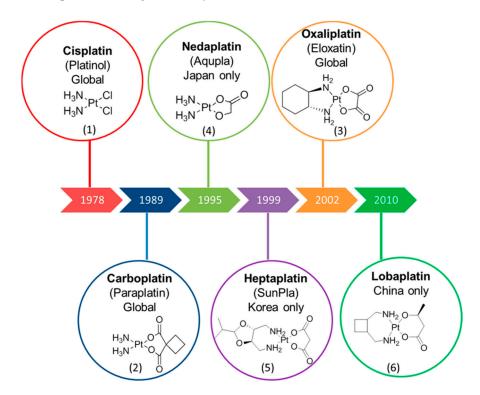


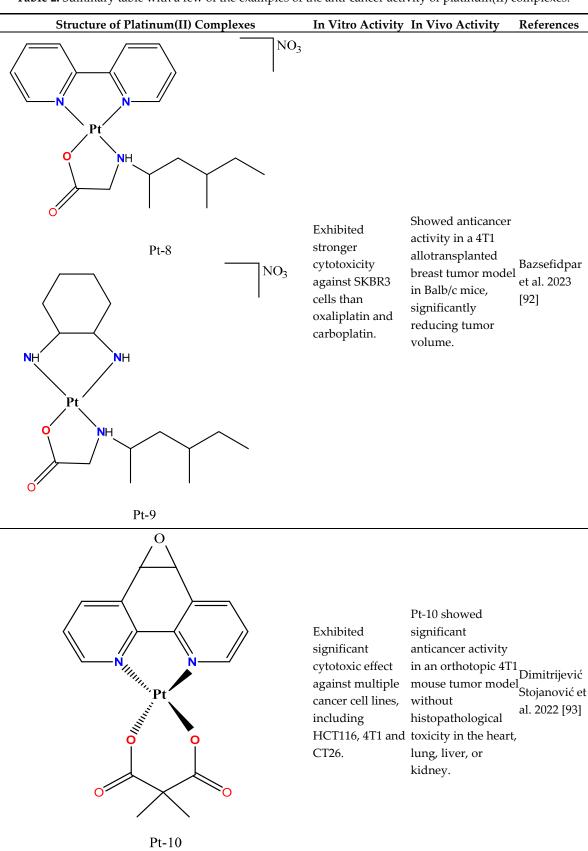
Figure 5. Platinum drugs in clinical use (with generic names in brackets), together with the years in which they received either global or limited regulatory approval [91].

Platinum(II)-Based Anti-Cancer Drugs

Recent studies have described a range of mononuclear Pt(II) complexes exhibiting potent anticancer activity. Selected examples of the anticancer properties of these platinum(II) complexes are summarized in Table 2. Bazsefidpar et al. obtained Pt-8 and Pt-9, incorporating 1,3-dimethylpentylglycine, with Pt-9 showing strong cytotoxicity (IC₅₀ = 15 μ M) against SKBR3 breast cancer cells and significant antitumor effects in 4T1 allograft mice [92]. Dimitrijević Stojanović et al. developed Pt-10 with a 2,2-dimethylmalonic acid ligand, demonstrating selective cytotoxicity and in vivo tumor suppression [93]. Qin et al. reported Pt-11 and Pt-12, a cryptolepine-based complexes, with superior cytotoxicity (IC₅₀ = 0.2 μ M) and apoptosis induction via mitochondrial pathways, reducing T-24 xenograft tumor growth more effectively than cisplatin [94]. Maciel et al. identified Pt-13, a naphthyl-substituted complex, highly selective against MDA-MB-231 cells and reducing xenograft tumor growth by 65.4% [95]. Ruiz et al. demonstrated that Pt-14, a hydroxyquinolate complex, impaired osteosarcoma cell viability and inhibited tumor growth without renal or hepatic toxicity [96]. Mo et al. synthesized Pt-15 and Pt-16, 8-hydroxyquinoline–tropolone derivatives, with

Pt-15 exhibiting potent cytotoxicity (IC₅₀ = $3.6 \mu M$), ROS generation, cell cycle arrest, and effective tumor suppression in vivo, comparable to cisplatin [97]. Collectively, these studies highlight the structural diversity and therapeutic potential of Pt(II) complexes as selective anticancer agents.

Table 2. Summary table with a few of the examples of the anti-cancer activity of platinum(II) complexes.

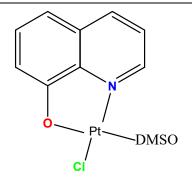


Induced more efficiently than cisplatin.

Administration of the Pt(II) complex co death in T-24 cells (2.0 mg/kg every 2 Qin et al. days) reduced T-24 2021 [94] xenograft growth in mice.

Pt-13 induced cytotoxicity in multiple tumor cell lines, including A549, PC3, MDA-MB-231, MCF-7, BXPC-3, and PBMC.

Strongly suppressed MDA-Maciel et al. MB-231 tumor 2022 [95] xenograft growth in BALB/c nude mice.

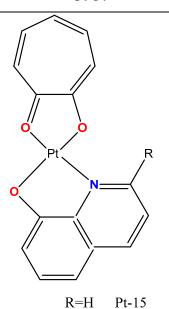


Pt-14

Quinolineplatinum complexes induced cytotoxicity in cisplatin-resistant human

osteosarcoma MG-63 cells.

Inhibited growth of human Ruiz et al. 2019 [96] osteosarcoma xenografts in mice.



Induced cytotoxicity in HeLa, A549, T24, and NCI-H460 cells more efficiently than cisplatin.

In female Balb/c nude mice, tumor xenograft growth Mo et al. was inhibited with 2021 [97] efficacy comparable to cisplatin.

R=CH₃ Pt-16

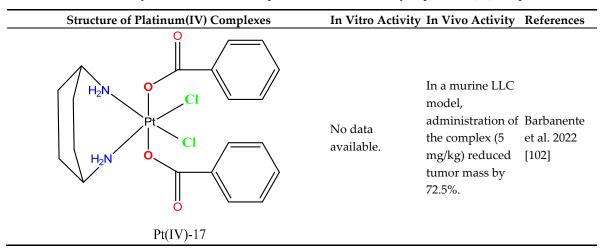
Franich et al. synthesized dinuclear cationic aqua Pt(II) complexes with pyridine-based bridges, demonstrating strong DNA binding, overcoming cisplatin resistance, and inhibiting tumor angiogenesis and melanoma metastasis in zebrafish-mouse xenograft models [98]. Gadre et al. developed heterobimetallic Pt(II)-ferrocene complexes that selectively targeted tumor cells via OCT2-mediated uptake, induced ROS-mediated non-apoptotic cell death, and suppressed A2780 xenograft tumors more effectively than oxaliplatin [99]. Hu et al. reported bis(N-heterocyclic carbene) Pt(II) complexes capable of overcoming cisplatin resistance, reducing NCI-H460 tumor growth by 70% in vivo through ASNS targeting [100]. Six Pt(II) complexes based on a naphthalenebenzimidazole scaffold exhibited IC50 values of 2.36–11.61 µM across eight cancer cell lines, outperforming cisplatin in SMMC-7721 and U251 cells [101]. Collectively, these studies highlight the structural diversity, enhanced selectivity, and potent anticancer activity of Pt(II) complexes, emphasizing the role of rational ligand design in developing next-generation platinum-based therapeutics.

In summary, recent advances in platinum-based complexes demonstrate that rational ligand design can significantly enhance anticancer efficacy, selectivity, and safety profiles compared to classical cisplatin. While numerous derivatives have shown promising in vitro and in vivo activity, challenges remain in optimizing pharmacokinetics, overcoming drug resistance, and ensuring minimal off-target toxicity. Future research should focus on systematic structure–activity relationship studies, targeted delivery strategies, and detailed mechanistic investigations to facilitate the translation of these novel Pt(II) complexes into clinically viable therapeutics.

Platinum(IV)-Based Anti-Cancer Drugs

Pt(IV) complexes represent a promising class of anticancer agents with octahedral geometry, greater kinetic inertness, and reduced off-target interactions compared to Pt(II) drugs. Pt(IV)-17 showed strong in vitro efficacy and reduced tumor mass by 72.5% in a Lewis Lung Carcinoma model, although neurotoxicity was observed [102]. Pt(IV)-18, a cisplatin/oxoplatin derivative incorporating a TDO inhibitor, demonstrated exceptional potency against TDO-overexpressing HepG2 cells (IC50 = 0.30 μ M), induced S-phase arrest, ROS generation, mitochondrial apoptosis, and enhanced antitumor immunity, reducing xenograft tumor growth by 70.5% [103]. Structure–activity studies indicated that mono-naproxen Pt(IV) derivatives, such as Pt(IV)-19, effectively overcame drug resistance and displayed strong cytotoxicity (IC50 ~5.4 μ M) with reduced toxicity in vivo [104]. Jin et al. developed Pt(IV)–naproxen derivatives (Pt(IV)-21 and Pt(IV)-22), with Pt(IV)-22 exhibiting potent cytotoxicity (IC50 = 0.16–0.34 μ M), significant tumor suppression in MDA-MB-231 xenografts, and anti-inflammatory effects without major toxicity [105,106]. These studies highlight Pt(IV) prodrugs as selective, efficacious anticancer agents with potential added immunomodulatory and anti-inflammatory benefits.

Table 3. Summary table with a few examples of anti-cancer activity of platinum(IV) complexes.



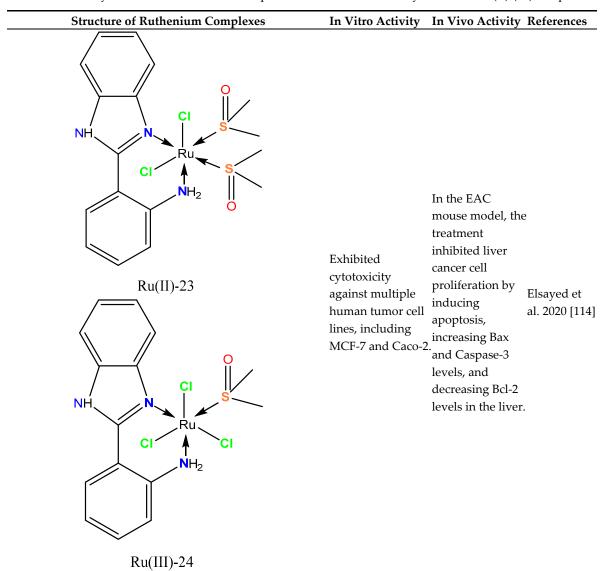
Cisplatin-derived Pt(IV) complexes incorporating medium-chain fatty acids as axial ligands, such as octanoate (OA) and its branched isomer valproate (VPA), have demonstrated remarkable antiproliferative activity in cellular studies [107,108]. Novohradsky and colleagues reported a compound, [Pt(IV)diOA], containing two axial OA ligands, which exhibited strong cytotoxic effects against various tumor cell lines [109].

Pt(IV)-22

Ruthenium-Based Anti-Cancer Compounds

Ruthenium-based compounds are extensively studied for therapeutic applications due to their ability to interact with biomolecules such as DNA and proteins. Under physiological conditions, Ru(II) (d⁶, diamagnetic) and Ru(III) (d⁵, paramagnetic) are stable, with Ru(II) being more reactive and exhibiting ligand exchange rates comparable to Pt(II). Ru(II)-arene complexes, including those with 5,7-dihalogenated-2-methyl-8-quinolinol or aryl-bis(imino) acenaphthene ligands, demonstrated selective cytotoxicity against HeLa and CT26 cells, induced ROS, inhibited migration, and reduced tumor growth in xenograft models [110,111]. Table 4 presents a few of the examples of the anti-cancer activity of ruthenium complexes. Acylthiourea- and 2-aminophenyl benzimidazole–containing Ru complexes showed enhanced distribution, DNA/protein interactions, and anticancer activity [112–114]. Polypyridyl Ru(II) complexes exhibited limited activity alone but showed strong cytotoxicity (IC $_{50}$ ~3.4 μ M) when liposome-encapsulated, inducing G2/M arrest, ROS generation, ferroptosis, and autophagy [115]. Incorporation of dipyridophenazine (dppz) ligands into Ru(II)-arene scaffolds formed reactive species capable of DNA binding and degradation, with p-cymene arene substitution enhancing activity 17-fold and improving selectivity in HCT116 cells [116,117]. These findings underscore the potential of Ru(II)-based complexes as selective and potent anticancer agents.

Table 4. Summary table with a few of the examples of the anti-cancer activity of ruthenium(II)/(III) complexes.



Alessio and Messori conducted a comparative analysis of landmark Ru(III) complexes, NAMI-A and KP1019/KP1339, emphasizing their pharmacological profiles, mechanisms of action, and clinical significance [118]. Ruthenium-based anticancer agents, including NAMI-A, KP1019, KP1339 (in clinical trials), and DW1/2 (preclinical), exhibit considerable therapeutic potential, with DW1/2 functioning as a protein kinase inhibitor [119,120]. New obtained Ru(II) complexes, such as 5-chloro-8-hydroxyquinoline–valine isomers and Ru(II) arene chlorido complexes, demonstrated strong cytotoxicity (IC $_{50}$ = 0.3–0.71 μ M), selectively induced apoptosis, and caused G2/M cell cycle arrest in various cancer cell lines, while sparing normal cells [121,122]. Additionally, cyclometalated Ru(II) and biotin-conjugated polypyridyl complexes exhibited improved solubility, stability, organelle targeting, and potential for phototherapeutic applications [123–125]. Collectively, these findings underscore the significant therapeutic promise of Ru-based complexes, although further research and clinical validation are required to facilitate their translation into effective cancer therapies.

Organic Compounds with Anti-Cancer Properties

Cancer continues to represent a major global health challenge, motivating the ongoing pursuit of safe and effective therapeutic strategies. Among therapeutic candidates, organic small molecules—particularly those derived from natural products, heterocyclic scaffolds, and rationally designed hybrids—have emerged as a cornerstone in modern medicinal chemistry. The attractiveness of these compounds stems from several intrinsic advantages: favorable pharmacokinetic and pharmacodynamic profiles, oral bioavailability, structural diversity, and synthetic accessibility [126]. Since 2017, drug discovery efforts have delivered a notable wave of small-molecule anticancer agents—including kinase inhibitors, PARP inhibitors, and novel purine hybrids—demonstrating improved potency, selectivity, and reduced systemic toxicity when compared to classical chemotherapies [127].

Natural products continue to serve as rich reservoirs for anticancer scaffolds. Plant-based small molecules, such as flavonoids and phytochemicals, have shown chemopreventive and therapeutic activity, particularly through kinase pathway modulation in precision oncology approaches [128]. Synthetic innovations are also accelerating progress—for instance, purine-based hybrids, incorporating structural features like chalcones or triazoles, have achieved potent activity across multiple cancer types in recent studies [129]. Overall, the synergy of natural product inspiration and synthetic design is generating versatile, multi-targeted organic compounds with promising anticancer activity, setting the stage for their potential translation into the clinic. Recently, Atanasov et al. reviewed current technological advances facilitating natural product-based drug discovery, highlighting selected applications and discussing key opportunities [130]. Newman and Cragg in 2020 quantified how often organic natural products underpin approved anticancer drugs [131]. Chunarkar-Patil et al. published a review of NP-derived small molecules and mechanisms in cancer [132]. Liu et al. reported a comprehensive map of approved and clinical-stage small-molecule cancer inhibitors [133]. Zhong and colleagues presented a review on targets, successes, and resistance for small-molecule oncology drugs [134]. Xue et al. focused on organic small-molecule-based nanomedicines and delivery [135]. Feng et al. explored emergent epitranscriptomic small molecules for cancer therapy [136]. Anticancer activities of natural and synthetic steroids was published by Mendoza Lara et al. [137]. This extensive review examined spirooxindole—a highly promising synthetic scaffold—exploring its diverse derivatives and their notable anticancer potential [138]. It presented structure-activity relationship (SAR) insights, covering mechanisms like cell cycle arrest, apoptosis, anti-angiogenesis, and anti-metastasis across multiple cancer types, including breast, lung, colon, and prostate [138]. Different authors focused on design and synthesis of organic molecules as antineoplastic agents [139–149].

Inorganic and Organic Compounds with Antimicrobial Properties

Saidin et al. presented a review captured a wide spectrum of antimicrobial strategies—including organic molecules (e.g., quaternary ammonium salts, guanidines, halogenated amines) and inorganic agents (including nanoparticles)—and discussed their mechanisms, stability, and applicability in biomedical contexts [150]. It's an excellent resource if you're looking to understand how both chemical domains contribute to combating bacterial infections. Both organic and inorganic antibacterial agents have gained significant attention as alternatives to conventional antibiotics, particularly in light of rising multidrug resistance. The review by Hess emphasized inorganic and organometallic antibacterials, highlighting rational design strategies that exploit metal-specific reactivity and redox properties to overcome bacterial defenses [151]. In contrast, the review of Saidin et al. provided a broader classification of both organic compounds (e.g., triclosan, polyaniline, chlorhexidine) and inorganic agents (e.g., silver, copper, zinc), focusing on their mechanisms of action and biomedical applications. Taken together, these works illustrate how combining the tunability of organic compounds with the unique physicochemical advantages of metal-based agents could yield synergistic antibacterial strategies, paving the way for next-generation therapeutics.

The development of antibacterial agents has increasingly focused on both organic and inorganic compounds, as well as hybrid systems, to combat the growing challenge of antimicrobial resistance. Inorganic compounds, particularly polyoxometalates, have shown promising antibacterial properties due to their structural diversity and ability to interact with bacterial membranes and enzymes [152]. Similarly, organometalated drugs and metal-based materials have been explored for their broad-spectrum activity, offering unique mechanisms of action compared to conventional antibiotics [153]. Organic approaches, on the other hand, include synthetic small molecules and naturally derived polymers with antibacterial effects, such as modified biopolymers that enhance stability and selectivity [154].

Gold(I/III)-Based Compounds with Antimicrobial Properties

Gold complexes, Au(I) and Au(III) in particular, have demonstrated promising antimicrobial activities against bacteria, fungi and even multidrug-resistant bacteria. The FDA-approved antiarthritic drug auranofin has demonstrated notable antibacterial activity, particularly against Gram-positive bacteria [155,156]. Specifically, auranofin exhibited a minimum inhibitory concentration (MIC) of 0.215-0.25 µg/mL against Staphylococcus aureus, whereas significantly higher MIC values were observed against Escherichia coli (31.25 µg/mL) and Pseudomonas aeruginosa (>250 µg/mL) [157]. Wiederholt et al. (2017) reported antifungal activity of auranofin against various Candida species, with MIC values ranging from 0.25 to 16 µg/mL [156]. Additionally, Torres et al. (2016) demonstrated that auranofin effectively disrupted biofilms of S. aureus and P. aeruginosa, with minimum biofilm eradication concentrations of 7.99 and 6.24 µg/mL, respectively [155]. Many authors have attempted to synthesize auranofin analogues in order to broaden and improve its antimicrobial spectrum [158–160]. Various other Au(I) complexes exhibited antimicrobial properties. Frik et al. (2012) synthesized posphine gold (I) complexes with activity against E. coli, Bacillus cereus, S. aureus and Saccharomyces cerevisiae [161]. Chen et al. (2023) demonstrated that a series of Au(I) selenium NHC complexes effectively inhibited multidrug-resistant bacteria, in some cases exhibiting markedly superior activity to auranofin both in vitro and in vivo [162]. Ndugire et al. (2022) synthesized phosphine-capped gold nanoclusters and glycosylated them to produce auranofin analogues with mixed TPPMS/Ac₄GlcSH ligand shells, enhancing activity against Gram-negative bacteria while reducing toxicity toward human A549 cells [163]. The proposed antibacterial mechanism is DNA degradation and irreversible inhibition of the cell's thioredoxin reductase activity, which leads to cell metabolism dysfunction due to oxidative stress [162,163]. Organometalic complexes with Au(III) have also been investigated for antimicrobial activity, although in a lesser extent than Au(I) comlexes. Cyclometalated complexes are the main focus of researchers because of their stability and chemical plasticity [164]. A gold (III) 1,2 thiolene cyclometalated complex exhibited activity against S. aureus and S. heamolyticus, as well as interference with the formation of biofilms by both staphyloccocal strains [165]. Chakraborty et al. (2021) reported on gold (III) complexes inhibiting S. aureus, B. subtilis and to a lesser extent - Enterococcus faecium and E. coli [166]. The Au(III) Nheterocyclic carbene complexes of Bussing et al. (2021) demonstrated activity against S. aureus, Klebsiella pneumoniae, E. faecium, E. coli, P. aeruginosa and Acinetobacter baumannii [167]. The precise mechanism of action of these complexes remains unclear; however, it is likely to involve disruption of cellular membranes [164].

Platinum (II/IV)-Based Compounds with Antimicrobial Activities

Platinum is also included in metal complexes with different ligands. The synthesized compounds are investigated for antimicrobial activity against various microorganisms. Pereira et al. (2020) examined Pt(II) complexes with adamantine derivatives and found that there was a significant improvement in the inhibitory effect against Gram-positive bacteria S. aureus and Bacillus cereus for all three complexes, and the Pt-memantine complex was effective against E. coli (MIC ≤ 0.14 mmol/L) [168]. In another study 3 cyclometalated complexes with Pt (II) were investigated for antibacterial activity against S. aureus and MRSA (Methicillin-resistant Staphylococcus aureus) [169] and all of them showed improved or comparable results to that of the ligand. Lunagariya et al. also observed improvement in the antimicrobial activity of their 5-quinoline 1,3,5-trisubstituted pyrazole based platinum(II) complexes in comparison with the ligand expressed by lower MICs [170]. The antibacterial properties of ciprofloxacine against Campylobacter jejuni were improved significantly (with an average 34.8-fold reduction in the MIC value) by the addition of a Pt(II) complex with 5amino-1,3,4-thiadiazole-2(3H)-thione and the complex by itself demonstrated a stronger effect than ciprofloxacine [171]. The proposed mechanisms for antimicrobial activity of the Pt(II) complexes is the Tweedy's chelate theory: chelation facilitates the penetration of the cell membrane by the complex [172].

Radić et al. investigated a Pt(IV) complex bearing a meso-1,2-diphenyl-ethylenediamin-N,N'-di-3-propanoate ligand against multiple microorganisms and observed low to moderate antimicrobial activity, with MIC values ranging from 125 μ g/mL to >1000 μ g/mL and MMC values from 500 μ g/mL to >1000 μ g/mL. At the tested concentrations, growth of clinical isolates of *S. aureus*, *E. coli*, *E. faecalis*, *Proteus mirabilis*, *Salmonella enterica*, *Aspergillus flavus* and *Candida albicans* was not inhibited [173]. A heteroscorpionate-derived Pt(IV) complex emerged as a promising therapeutic candidate against methicillin-resistant *Staphylococcus aureus* (MRSA) [174], inhibiting the growth of MRSA planktonic cells (with an MIC eight times lower than that of the free ligand) and reducing biofilm formation in both conventional biofilm-inducing media and wound-like environments. Pt(IV) complexes incorporating N-alkylphenothiazines also demonstrated activity against bacilli, MRSA, and *E. coli* [175]. Additionally, Frei et al. (2021) evaluated 14 platinum(IV) cyclooctadiene complexes, reporting activity primarily against Gram-positive bacteria [176] and ten of these compounds exhibited some activity against the Gram-positive bacteria included in the panel and/or *C. albicans* and *Candida neoformans* with two of them showing excellent effect on *S. aureus, Staphylococcus epidermidis*, *B. subtilis* and MRSA.

Ruthenium(II/III)-Based Compounds with Antimicrobial Activities

Ruthenium is the most common element found in organometal complexes [177]. Multiple studies have investigated Ru(II) complexes with different compositions – mononuclear, [178–180], polynuclear [181,182], hetero-metalic complexes, Ru-based carbon-monoxide-releasing molecules [183,184]. Wang et al. explored the in vitro antibacterial effect of four mononuclear Ru(II) complexes against S. aureus and detected MICs between 0.0156 and 0.2500 mg/mL. The most effective complex was further investigated and the authors determined, that it interrupted biofilm formation and toxin secretion by S. aureus, enhanced the antibiotic activity of 9 commonly used antibiotics and ointments containing this complexes were highly active against mouse skin infections [185]. A 3,3'-dicarboxy-2,2'- bipyridine complex with Ru(II) displayed MIC of 35 µg/mL against S. aureus and 35 µg/mL against E. coli [186]. Huang et al. reported on ruthenium complexes containing phenylseleny with excellent antimicrobial activity against S. aureus in vitro (MIC 1.56-6.25 μg/mL), biofilm inhibition and the ability to clear infections in vivo in a mouse and laravae model [187]. The arene-Ru(II) complex synthesized by Namiecińska et al. (2020) inhibited the growth of Gram-positive bacteria such as S. aureus, S. epidermidis and E. faecalis, but not – Gram-negative and yeasts [188]. Zhou et al. (2025) determined, that and aromatic ruthenium (II) complex demonstrated in vitro significant activity against S. aureus, and the infection in vivo in wound and a sepsis models was effectively inhibited. At a molecular level the complex disrupted biofilm formation and decreased toxin secretion by S. aureus [189]. Gorle et al. (2014) investigated the antimicrobial activity of tri- and tetranuclear polypyridyl ruthenium(II) complexes against four bacterial strains, including Gram-negative E. coli and P. aeruginosa and methicillin-resistant S. aureus (MRSA), as well as Gram-positive S. aureus [190]. The complexes exhibited excellent antimicrobial activity with rapid uptake and high level of accumulation of the tetranuclear complexes in bacteria cells. In recent studies CORMs have displayed bactericidal activity against antibiotic-resistant P. aeruginosa [191], H. pylori [192], and E. coli [193] strains. Stringer et al. (2017) synthesized a heterobimetallic complex from a Schiff base-derived isonicotinyl ferrocene complex using ruthenium dimers, which exhibited activity against Mycobacterium tuberculosis [194]. The antimicrobial activity of ruthenium(III) complexes is less studied. Tao et al. investigated ruthenium coordination polymer composites incorporating chitosan quaternary ammonium polymers and shikimic acid, which demonstrated enhanced antimicrobial activity against S. aureus compared to the free ligand and retained efficacy in time-kill assays [195]. These composites also inhibited S. aureus biofilm formation in a dose-dependent manner, likely through disruption of cell membrane integrity, inhibition of Ca²⁺-Mg²⁺-ATPase activity, and modulation of intracellular Ca²⁺ levels. Similarly, ruthenium(III) complexes with Schiff base ligands exhibited greater antibacterial activity than their corresponding free ligands under comparable conditions [196]. Recent reviews highlight the importance of combining organic and inorganic

strategies for biomedical applications. Saidin et al. emphasized that hybrid organic-inorganic antibacterial systems can improve therapeutic efficiency by enhancing bioavailability, targeting, and reducing toxicity [150]. Natural and semi-synthetic compounds, such as polyphenols and essential oil derivatives, are also being integrated with nanomaterials to yield synergistic antibacterial effects [197,198]. More recently, novel antibacterial agents with new mechanisms, such as cell wall biosynthesis disruption or membrane destabilization, have been reported, providing alternatives to overcome multidrug-resistant strains [199,200]. Importantly, applied studies, such as the use of compound organic acids to treat *Staphylococcus aureus*-induced infections in poultry, demonstrate the translational potential of organic antibacterial strategies in clinical and agricultural settings [201]. Overall, the integration of organic, inorganic, and hybrid antibacterial compounds presents a promising frontier in drug development, aiming to deliver safe, effective, and resistance-evading therapies. Future research should focus on structure-activity relationships, targeted delivery mechanisms, and comprehensive pharmacological evaluations to accelerate clinical translation.

Inorganic and Organic Compounds with Anti-Inflammatory Properties

The search for effective anti-inflammatory agents increasingly spans both organic and inorganic chemistry, combining traditional and novel approaches.

Organic Heterocycles—Pyrimidines. Synthetic pyrimidines have shown considerable promise as anti-inflammatory agents. Their structure–activity relationships (SARs) highlight activity against key mediators, including prostaglandin E_2 (PGE₂), inducible nitric oxide synthase (iNOS), NF- κ B, TNF- α , leukotrienes, and multiple interleukins, underscoring their therapeutic potential [202]. Gallium-based agents have demonstrated consistent anti-inflammatory activity across preclinical studies between 2000–2019, with evidence for their action through diverse inflammatory pathways. These findings support further development of gallium compounds as anti-inflammatory therapeutics [203].

Organometallic NSAID Complexes. The coordination of non-steroidal anti-inflammatory drugs (NSAIDs) with metal ions has emerged as a promising strategy to enhance therapeutic potency while mitigating adverse effects. For example, a copper–aspirin complex demonstrated enhanced COX-2 inhibition with fewer gastrointestinal side effects compared to aspirin alone. Similarly, zinc–aceclofenac complexes were reported to reduce gastric inflammation by masking the drug's carboxyl groups [204].

Flavonoids and Metal Complexes. Flavonoids, chromones, and coumarins—and their respective metal complexes—exhibit anti-inflammatory, antioxidant, and antimicrobial activity. Metal conjugation often improves their stability and biological performance, suggesting significant therapeutic value [205].

Organosulfur Natural Products. Natural organosulfur compounds (OSCs), widely found in garlic and onions, downregulate inflammatory mediators (NO, PGE2, IL-1 β , IL-6, TNF- α , IL-17) and suppress NF- κ B signaling, providing strong evidence of their anti-inflammatory and antioxidant efficacy [206]. Thirteen heterocyclic coxib-like 4,5-diarylfuran-3(2H)-ones and their fused phenanthro [9,10-b]furan-3-one derivatives were synthesized and evaluated for anti-inflammatory activity, COX-1/2 inhibition, and cytotoxicity against MCF-7 and HSC-3 cell lines [207]. Among these, the fluorinated –SOMe furan-3(2H)-one exhibited the highest activity, with a COX-1 IC50 of 2.8 μ M, 54% anti-inflammatory effect, and IC50 values of 10 μ M and 7.5 μ M against MCF-7 and HSC-3 cells, respectively. This compound also displayed synergistic effects with gefitinib and 5-fluorouracil, with a phenanthrene derivative showing the most pronounced synergy [207].

Nanomaterials. Inorganic nanostructures are also being investigated for inflammation control. Fullerene-like tungsten disulfide (IF-WS₂) nanoparticles have been shown to reduce the expression of pro-inflammatory cytokines, including TNF- α , IL-1 β , IL-8, and MCP-1, in peripheral blood mononuclear cells, highlighting their immunomodulatory potential [208]. Mebeverine hydrochloride, an antispasmodic agent that regulates bowel movements and relaxes intestinal smooth muscle, is limited in clinical use due to certain adverse effects. In this context, Stoyanova et

al. investigated the effects of previously synthesized MBH-loaded silver nanoparticles (AgNPs) on smooth muscle contractility and their anti-inflammatory properties, proposing them as a potential alternative delivery system [209].

Ivanov et al. synthesized new compounds by combining 2-aminobenzothiazole with various profens [210]. Derivatives 3b (HPSA IC $_{50}$ = 60.24 µg/mL) and 3c (HPSA IC $_{50}$ = 67.71 µg/mL) exhibited strong antioxidant activity and significant anti-inflammatory effects, with IAD values of 54.64 µg/mL and 64.44 µg/mL, respectively [210]. Dimitrova and co-worker reported the synthesis through N,N'-dicyclohexylcarbodiimide-mediated and characterization of five trimetazidine–profen hybrids [211]. Antioxidant activity (HRSA) and anti-inflammatory potential (IAD) were assessed [211]. Ivanov et al. synthesized five novel compounds by conjugating flurbiprofen with various substituted 2-phenethylamines [212]. Molecular docking studies further elucidated the in vitro results, providing insights into the molecular mechanisms underlying their observed biological activities (see Figure 6).

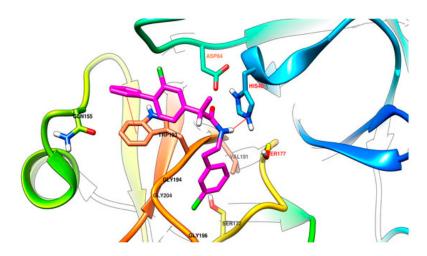


Figure 6. Predicted binding of compound (S)-4e within the active site of trypsin, as determined by AutoDock Vina in rigid mode [212]. The compound engages in a π – π stacking interaction with Trp193, donates a hydrogen bond from its amide group to His40, and positions its meta-chlorobenzene moiety within a pocket formed by three glycines, a valine, and a serine. The figure illustrates the protein's tertiary structure, key heavy atoms, and relevant hydrogen atoms.

Compounds 4a–e exhibit pronounced intravenous toxicity, with 4e being four times more toxic than flurbiprofen [212]. The presence of methoxy substituents, particularly in 4b-d, correlates with reduced toxicity. Due to complete bioavailability, intravenous administration results in lower lethal doses. Among the series, 4d shows the lowest intraperitoneal toxicity (toxicity order: Flu > 4b > 4c > 4a > 4e > 4d). In contrast, oral administration of 4b-d markedly decreases toxicity—by more than threefold compared with flurbiprofen-highlighting the oral route as a safer and more favorable mode of delivery [212]. Polyphenolic fractions of Helichrysum italicum (hexane, chloroform, EtOAc, butanol) were analyzed by HPLC-PDA and UHPLC-MS/MS, identifying 60 compounds (several reported for the first time) by Bojilov et al. [213]. The EtOAc fraction showed strongest antioxidant/nitrosative activity, while hexane and chloroform fractions exhibited superior antiinflammatory effects. It should be noted that all fractions exhibited anti-arthritic potential [213]. The synthesis of four newly hybrid molecules, derived from ketoprofen (2-(3-benzoylphenyl)propanoic acid) and nitrogen-containing heterocyclic compounds-including piperidine, pyrrolidine, 1,2,3,4tetrahydroquinoline, and 1,2,3,4-tetrahydroisoquinoline—has been reported [214]. All compounds were evaluated for their in vitro anti-inflammatory and antioxidant activities. Additionally, Manolov et al. described the synthesis of novel hybrid molecules combining amphetamine with ibuprofen, flurbiprofen, ketoprofen, naproxen, and carprofen [215]. The in vitro inhibitory activity of the synthesized compounds against albumin denaturation was evaluated, revealing significant effects. The IC₅₀ values of the resulting amphetamine–profen derivatives were found to range between 92.81

and 159.87 µg/mL. The findings reported by Panova et al. suggest that *Moringa oleifera* possesses considerable potential as a candidate for antimicrobial, antioxidant, anti-inflammatory, and antispasmodic applications, supporting its use in the development of alternative pharmaceutical and nutraceutical products [216]. Todorova and co-workers present the synthesis of a new styryl quinolinium derivative, as well as an evaluation of its anti-inflammatory and antioxidant activities [217]. Stoyanova et al. synthesized new mebeverine analogs and evaluated their spasmolytic properties ex vivo, as well as their anti-inflammatory activities both ex vivo and in vitro [218]. Gerasimova et al. investigated the metabolic profile, elemental composition antimicrobial, antioxidant and anti-inflammatory activities of *Passiflora caerulea L.* cultivated in Bulgaria [219]. Their analyses revealed that glucose, fructose, and sucrose were present in the pulp and leaves, whereas amino acids were predominantly found in the fruits.

2. Conclusions

This study demonstrates that both inorganic and organic compounds possess significant therapeutic potential, including anticancer, antimicrobial, and anti-inflammatory activities. The main emphasis is on the antitumor effect 89 articles of inorganic and organic compounds, 53 with antimicrobial action and 17 - anti-inflammatory activities. Transition metal-based inorganic complexes (especially with Au(I/III), Pt(II/IV), Ru(II/III)) and bioactive organic derivatives showed promising interactions with biomolecular targets. These findings underscore the value of integrating synthetic chemistry and natural compounds with biological evaluation to guide the development of effective drug candidates and support the ongoing exploration of metallodrugs and organic therapeutics for clinical applications.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

¹ H NMR	proton nuclear magnetic resonance
¹³ C NMR	carbon-13 nuclear magnetic resonance

ESI-HRMS electrospray ionization high-resolution mass spectrometry

ESI-MS electrospray ionization mass spectrometry

FT-IR fourier transform infrared

ICP-MS inductively coupled plasma mass spectrometry

TrxR thioredoxin reductase
DMSO dimethyl sulfoxide
AuNPs gold nano particles
NP nano particle

ATP adenosine triphosphate PEG polyethylene glycol

PET positron emission tomography

MM multiple myeloma
HCC hepatocellular carcinoma
ROS reactive oxygen species
FDA Food and Drug Administration
4T1 mouse mammary carcinoma cell line

Bcl-2 B-cell lymphoma 2

Apaf-1 Apoptotic Protease-Activating Factor 1



MDA-MB-231 A human breast adenocarcinoma cell line established from a patient with

metastatic mammary adenocarcinoma

MCF-7 Another human breast cancer cell line used in cancer research

A549 A human lung carcinoma cell line
PC3 A human prostate cancer cell line
BXPC-3 A human pancreatic cancer cell line
PBMCn Peripheral Blood Mononuclear Cells
SAR Structure—activity relationship
CT-DNA calf thymus-Deoxyribonucleic acid
MMP mitochondrial membrane potential

CDK1 cyclin-dependent kinase 1 Cdc25A cell division cycle 25 A

B16-F10 a specific murine melanoma cell line derived from the B16 tumor line

A2780 ovarian cancer cell line ASNS asparagine synthetase

HepG2 A human liver carcinoma cell line

HeLa A common human cervical cancer cell line

SKOV3 A human ovarian cancer cell line

BEL-7404 A human hepatocellular carcinoma cell line NCI-H460 A human large cell lung carcinoma cell line

U251 A human glioblastoma cell line

SMMC-7721 A human hepatocellular carcinoma cell line

LLC Lewis Lung Carcinoma

C57BL inbred laboratory mouse strain
TDO tryptophan-2,3-dioxygenase
AHR aryl hydrocarbon receptor

NSAIDs non-steroidal anti-inflammatory drugs

COX-2 cyclooxygenase-2
COXs cyclooxygenases
IL interleukin
OA octanoate

HL-7702 non-malignant human liver cells

CT26 murine (mouse) cell line representing a highly immunogenic colorectal

carcinoma

SGC-7901 human gastric cancer cell line

HCT116 human colorectal cell line
HSA human serum albumin
AIE aggregation-induced emission
PARP poly (ADP-ribose) polymerase
MIC minimum inhibitory concentration
TPPMS triphenylphosphine monosulfonate
MMCs minimum microbiocidal concentration

dipyridophenazine

MRSA Methicillin-Resistant *Staphylococcus Aureus*Ca²⁺-Mg²⁺-ATPase Calcium Magnesium adenosine triphosphatase

 PGE_2 prostaglandin E_2 iNOS nitric oxide synthase

TNF-α Tumor Necrosis Factor-alpha

NF-κB Nuclear Factor kappa-light-chain-enhancer of activated B cells

MCP-1 Monocyte Chemoattractant Protein-1

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dppz

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