

# Different Health-Beneficial Pharmacological Effects of Metal-Based Organic Complexes

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## Abstract

## Review Article

Current study aims to summarise the different health-beneficial potential activity of non-platinum metal-based organic compounds. Literature analysis shows that the organic complexes of Ag, Au, Co, Cu, Fe, Mn, Mo, Ni, Zn, Ce, Ga, Gd, Ir, Os, Pd, Re, Rh, Ru, Ti, V, have been investigated to possess different pharmacological action. The more pronounced effects of metal complexes are combinations of anticancer and the following different activities: 1) anti-Alzheimer: Co, Cu, Ni, Pd, Ru, V; 2) antioxidant: Co, Cu, Fe, Ni, Zn, Mn, Ce, Nd, Ga, La; 3) antimicrobial: Ag, Au, Cr, Co, Cu, Fe, Mn, Ni, Zn, Ga, Ir, La, Pd, Ru; 4) antimalarial: Au, Co, Cu, Fe, Zn, Ga, Os, Pd, Rh, Ru; 5) anti-*Mycobacterium tuberculosis*: Cu, Fe, Os, Ru; 6) antifungal: Co, Cu, Ni, Ru, Pd; 7) anti-Leishmanial: Au, Ir, Ru, Os, Pd, La; 8) antitrypanosomal: B, Ir, Os, Pd; 9) antiinflammatory: Co, Cu, Mn, Ni, Ru; 10) anti-rheumatic: Au. Schiff bases metal agents possess antimicrobial, antifungal, antiviral, anti-inflammatory, antioxidant, and anticancer activities. N-heterocyclic carbene derivatives are included as ligands in Ag, Au, and Pd complexes with anticancer, and antimicrobial activity. An important trend in the investigation of novel antineoplastic agents is the development of arene complexes, derivatives of Ferrocene, and scorpionates, dinuclear complexes, mixed-ligand strategy. An important perspective trend is the development of natural product-conjugated metal complexes for cancer therapy with ligands from plant origin as Ferrocene podophyllotoxin, Ferrocene conjugates with flavonoids, Ru(II) complexes with 18 $\beta$ -glycyrrhetic acid, naphthoquinone/p-cymene, Curcumin metal-based complexes.

**Keywords:** Metal-organic complexes; pharmacological activity, health benefit.**Copyright © 2026 The Author(s):** This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

## INTRODUCTION

### I. Pharmacological activities of metal-based complexes

Different investigated metal-organic complexes have been reported to be promising agents for biomedical applications [1] in medicine and pharmacy [2]. The possibilities of medicinal applications in the therapy of coordination complexes are increased [3]. Due to their specific mechanisms of action and different pharmacological activities [4], metallopharmaceuticals

provide new trends for scientific research [5] and for perspectives in the discovery and development [6] of drug design [7]. Metal-based complexes can be divided in accordance with the type of metal, type of ligand, and pharmacological activity.

In Table 1. are summarised metals, whose complexes with different ligands have shown potential activity against different diseases.

**Table 1: Pharmacological activities of metal-based complexes**

Metal	Pharmacological effect
Ag	anticancer [8-12], antimicrobial [13,14]
Au	anticancer [8-10,15-20], anti-rheumatic [4], antimicrobial [21-23], antimalarial [24], anti-Leishmanial [4]
B	multiple myeloma, antitrypanosomal [4]
Cr	anticancer [25], antimicrobial [26-28]
Co	anticancer [29-36], antioxidant [4], anti-Alzheimer [37], anti-inflammatory [38], antimicrobial [39-40], antifungal [3], antimalarial [41]

Cu	anticancer [42,43], antioxidant [4], anti-Alzheimer [44], anti-inflammatory [45], antimicrobial [26,27,40,46,47], anti- <i>Mycobacterium tuberculosis</i> [48], antifungal [3], antimalarial [41]
Fe	anticancer [8,49,50], antioxidant [4], antidiabetic [51], antimicrobial [26-28], anti- <i>Mycobacterium tuberculosis</i> [52], antimalarial [41]
Mo	anticancer [8,53], antidiabetic [1,2]
Mn	anticancer [8], antioxidant [54], antiinflammatory [1], antimicrobial [28,55]
Ni	anticancer [8,56,57], antioxidant [1], anti-Alzheimer [37], anti-inflammatory [4], antimicrobial [58], antifungal [3]
Zn	anticancer [8,59-61], antioxidant [1], antidiabetic [1,2], antimicrobial [40,62], antimalarial [24]
Ce	anticancer [8,63,64], antioxidant [65]
Ga	anticancer [8], antioxidant [66], antimicrobial [67-69], antimalarial [24]
Ir	anticancer [8,70], antibacterial [71], anti-Leishmanial [4], antitrypanosomal [72]
La	anticancer [73], antioxidant [66,74], antimicrobial [75], anti-Leishmanial [76]
Nd	anticancer [64], antioxidant [65]
Os	anticancer [8,70], antimalarial [24], anti-Leishmanial [1], antitrypanosomal [72], anti- <i>Mycobacterium tuberculosis</i> [77]
Pd	anticancer [8], anti-Alzheimer [37], antimicrobial, antifungal [40], antimalarial [24], antitrypanosomal [72]
Rh	anticancer [8,78-80], antimicrobial [81]
Ru	anticancer [8,82-95], anti-Alzheimer [96], anti-inflammatory [45], antimicrobial [97], anti- <i>Mycobacterium tuberculosis</i> , antifungal, antiamoebic, antimalarial and anti-Chagas disease [98], anti-Leishmanial [4]
V	anticancer [8], anti-Alzheimer [99], antidiabetic [99]

The more pronounced different effects of metal complexes are combinations of anticancer and the following different activities:

- 1) anti-Alzheimer : Co [37], Cu [44], Ni [37], Pd [74], Ru [96], V [99];
- 2) antioxidant: Co, Cu, Fe [4], Ni, Zn [4], Mn [54], Ce, Nd [65], Ga [66], La [66, 74];
- 3) antimicrobial: Ag [13,14], Au [21-23], Cr [26-28], Co [39,40], Cu [26,27,40,46,47], Fe [26-28], Mn [28,55], Ni [58], Zn [40,55,62], Ga [67-69], Ir [71], La [75], Pd [40], Ru [97]; antimalarial: Au [24], Co, Cu, Fe [41], Zn, Ga, Os, Pd [24];
- 4) anti-*Mycobacterium tuberculosis*: Cu [48], Fe [52], Os [77];
- 5) antifungal: Co, Cu, Ni [3], Pd [40];
- 6) anti-Leishmanial: Au, Ir, Ru [4], Os, Pd, La [76];
- 7) antitrypanosomal: B [4], Ir, Os, Pd [72];
- 8) antiinflammatory: Co [38], Cu [45], Mn, Ni [4], Ru [45];
- 9) anti-rheumatic: Au [4].

Table 2. presents different pharmacological activities of metal complexes with specific ligands.

**Table 2: Different pharmacological activities of metal complexes with specific ligands**

Metal	Ligand	Pharmacological effect
Ag(I)	N-heterocyclic carbenes [100]	anticancer, antioxidant
Co (III)	2-acetylpyridine thiosemicarbazones [101] N-heterocyclic carbenes	anticancer, antioxidant
Cr (II)	picolinate, dipicolinate, oxalate, 2,2'-bipyridine 4,4'-dimethoxy-2,2'-bipyridine [102]	anticancer, antioxidant antimicrobial
Cu(I)	5-dimethyl-2-phenyl-4-[(pyridin-2-ylmethylene)-amino]-1,2-dihydro-pyrazol-3-one Schiff base [103]	anticancer, antioxidant
Cu(II)	complexes of dien and its Schiff dibases with heterocyclic aldehydes and 2-amino-2-thiazoline [104]	anticancer, anti-inflammatory
Ni (II)	Macrocyclic complex [105]	anticancer, antioxidant
Zn (II)	S-methyl dithiocarbazone Schiff base [106]	anticancer, antimicrobial
Pd (II)	3-methoxy salicylaldehyde-thiosemicarbazones [107]	anticancer, antibacterial
Pd (II)	thiosemicarbazones [108] adamantloylhydrazone-diphenylphosphino) benzaldehyde [109]	anticancer, antiviral
Pd (II)	N, N'-ligands derived from pyrazole [110] C,N,N'- ligands derived from pyrazole [110]	anticancer, antimalarial
Ag(I), Au(I), Pd(II)	N-heterocyclic carbene complexes [111]	anticancer, antimicrobial
Cu (II), Co (II)	Antipyrine [112]	anticancer, antioxidant

Cu (II), Ni (II)	2-[3-methyl-2-thienylmethylene] hydrazine carboxamide [113]	anticancer, antimicrobial antifungal
Ni (II), Pd (II)	[(1 <i>H</i> -1,2,4-triazole-3-ylimino)methyl]naphthalene-2-ol [114]	anticancer, antioxidant
Mn (III), Zn (II)	macrocyclic ligands [115]	anticancer, antioxidant
Co(II), Cu(II) Ni(II), Zn(II)	N-isonicotinoyl-N'-(3-methoxy-2-hydroxybenzaldehyde)- hydrazone [116]	anticancer, antimicrobial
Co(II), Cu(II) Ni(II), Zn(II)	8-hydroxyquinoline [117] 2-hydroxynaphthaldehyde; salicylaldehyde hydrazones [117] 1,10-phenanthroline/4-nitrophenyl)quinoxaline-2,3-diamine [118]	anticancer, antioxidant antimicrobial
Co(II), Cu(II), Ni(II), Zn(II), Mn(II)	N-(furan-2-yl-methylene)quinolin-8-amine [119]	anticancer, antioxidant, antimicrobial

Schiff base metal agents possess antimicrobial, antifungal, antiviral, anti-inflammatory, antioxidant, and anticancer activities [4]. N-heterocyclic carbene derivatives [111] are included as ligands in Ag, Au, and Pd complexes with anticancer, and antimicrobial activity. The same effects were investigated in Co (II), Cu (II), Ni (II), and Zn (II) compounds with a hydrazone derivative as the ligand [116]. Anticancer and antioxidant effects display complexes of Cu (II) and Co (II) with Antipyrine [112], Ni (II), and Pd (II) with a naphthalene derivative [114], and Mn (III), Zn (II) with macrocyclic ligands [115].

## II. non-platinum metal-based complexes as potential anticancer agents

### II.1. Type of metals included in the chemical structure of anticancer metal-based complexes with antiproliferative activity

Complexes of the following metals are potential therapeutic agents for medical applications due to possess antiproliferative activity [8]: Ag(I) [9,10], Au(I) [10], Au(III) [13], Ce(III) [63], Co(II), Co(III) [29,30], Cr(III) [120], Cu(II) [42], Fe(III) [49,50], Mo(II) [53], Ni(II) [56], Zn(II) [59], Ce(IV) [64], Eu(III) [73], Ga(III) [1], Ir(III) [70,71,121], Nd(III) [64], Os(II) [71, 121, 122], Re(I) [71, 123-124], Rh(III) [78, 125], Ru(II), Ru(III) [82-84,121,122], Ti(IV) [126], V(IV) [127].

### II.2. Type of ligands included in the chemical structure of anticancer metal-based complexes with antiproliferative activity

#### II.2.1. Common ligands in the chemical structure of metal-based complexes

The most common ligands included in the structure of metal complexes are presented in Table 3.

**Table 3. Common ligands included in the chemical structure of metal-based complexes.**

Ligands - derivatives of:	Metals
pyridine	Ag(I) [11], Au(III) [19], Co(III) [34], Zn(II) [60], Rh(III) [80], Ru(II) [89-91]
pyrazine	Ag(I) [9]
imidazole	Ag(I) [12]
benzimidazole	Cu (II) [43]
bis-benzimidazole	Zn (II) [59]
naphthopyrane	Ru (II) [93]
oxadiazole	Ag(I) [10], Au(I) [17]
quinoline:	Co (III) [36]
1,10-phenanthroline	Co (III) [35]
porphyrin	Au (III) [15]
hematoporphyrin IX	Au (II) [18]
thiosemicarbazone	Co (III) [34], Zn(II) [60]

Ligands such as Schiff bases and N-heterocyclic carbene derivatives are also the most common. Schiff base metal agents and N-heterocyclic carbene derivatives belong to the most investigated types of anticancer organometal compounds [128]. Schiff bases of pyrazine and thiazole: Ag(I) [9], and benzimidazole: Cu (II) [43] have been shown to exert antiproliferative properties.

Very often in structures of organic complexes of Ag(I) [10], Au(I) [10, 17], Ni(II) [57], and Ir(I) [71] are included N-heterocyclic carbenes, with substituents as 1,2,4-oxadiazole in Ag(I) [10] and Au(I) [17] agents, 4,5-dichloro-1*H*-imidazole in Ag(I) compounds [12], and Caffeine-based N-heterocyclic carbenes in Au(I) organometal agents [16]. Table 4. presents anticancer complexes of metals with specific ligands.

**Table 4: Anticancer complexes of metals with specific ligands.**

Metal	Ligand
Ag(I)	pyridine 2,6-derivatives [11]; pyrazine and thiazole Schiff bases [9] N-heterocyclic carbenes with 1,2,4-oxadiazole substituents [10] N-heterocyclic carbenes with 4,5-dichloro-1H-imidazole [12]
Au(I)	Caffeine-based N-heterocyclic carbenes [16] N-heterocyclic carbenes with 1,2,4-oxadiazole substituents [10,17]
Au (II)	hematoporphyrin IX [18]
Au (III)	bipyridine [19]; 2-[(dimethylamino)methyl] phenyl [20]; porphyrin [15]
Co(III)	acetylene-hexacarbonyl complexes [31]; acetylsalicylic acid - alkyne complexes [32] enkephalin-alkyne-carbonyl conjugates [33]; 2-acetylpyridine thiosemicarbazones [34]; 1,10-phenanthroline-5,6-dione [35]; 5-chloro-8-hydroxyquinolines [36] 2-[[2-(dimethylamino)ethyl]imino]methyl]-6-methoxyphenol [1]
Cu(I)	triazol-dihydrobis((3-nitro-1,2,4-triazolyl) borate [129] Adamantane- N-methyl-1,3,5-triaza-7-phosphoadamantane [130]
Cu (II)	N,N'-bis(substituted oxamides [131]
Cr (III)	tricarbonyl arene chromium [120]
Mo (II)	allyl dicarbonyl complexes with N-N coligands [53]
Ni (II)	N-heterocyclic carbenes [57]; triazine [56]
Zn (II)	bis-benzimidazole [59] 2-acetyl pyridine 1-(4-fluorophenyl)-piperazinyl thiosemicarbazone [60=108]; salicylaldehyde [61]
Ce (III)	bis-coumarins [63-64]
Eu (III)	5-Fluorouracil [73]
Ir(I)	N-heterocyclic carbenes [71]
Ir(III)	benzofuran [123]; pyridine-indole [132]
La (III)	5-Fluorouracil [73]
Nd (III)	bis-coumarins [64]
Os (II)	arene-picolinate derivatives [133]
Re(I)	alkoxy- and hydroxyl- carbonyl complexes [134] carbonyl 2-(dimethylamino) ethoxide complexes [135] phosphine-derivatized amines [136]
Rh (III)	Ferrocene [79]; polypyridyl [80]
Ru (II)	amino acids [85]; glycyrrhetic acid [86]; diamines [87] and diaminotriazines [88]; pyridine [89,90]; pyridine-Ferrocene [91]; naphthoquinone complexes with p-cymene [92]; naphthopyrans [93]; triphenylphosphine complexes [94]; Curcumin [95]

Complexes of more than one different metal with the same type of ligand possess properties as anticancer agents (Table 5.). Mercaptopyrimidine derivative is included as an equal ligand in both Ag(I), and Pd (II) organic complexes [137]. The most common used ligands are derivatives of pyridine: Ag(I), Pd (II)

[137]; pyrrolidine: Cu (II), Zu (II) [138]; triazine: Rh(I), Ru (II) [139]; piperidine: Zn (II), Pd (II) [140]. The most investigated potential anticancer agents of different metals with the same specific ligand are complexes of Co (II), Ni (II), Cu (II), and Zn (II) with Schiff bases of quinoline, and pyridine derivatives [141]

**Table 5: Anticancer complexes of different metals with equal ligands**

Metal	Ligand
Ag(I), Pd (II)	4,6-diamino-5-hydroxy-2-mercaptopyrimidine [137]; 2,2'-bipyridyl [137]
Cu(II), Zu (II)	pyrrolidine dithiocarbamate [138]
Rh(I), Ru (II)	2-amino-4-phenylamino-6-(2-pyridyl)-1,3,5-triazine [139]
Zn(II), Pd (II)	dipiperidine-2-carboxylic acid [140]
Co(II), Ni (II), Cu(II), Zn (II)	Schiff bases of 3-formyl quinoline and 2,6-diaminopyridine [141] Schiff bases of 2-mercapto-3-formyl quinoline with 2,6-diaminopyridine [1] schiff bases of 2-hydroxy-3-formylquinoline with 2,6-diaminopyridine [1]

Cu (II) complexes are the more suitable example of complexes of the same metal with [different ligands with anticancer activity. The most common

ligands are derivatives of pyrrolidine, pyridine, benzimidazoles, chinolone, purine or hydrazones, oximes, and thiosemicarbazones (Table 6.)

**Table 6: Anticancer activity of Cu (II) complexes with specific different ligands**

	<b>Ligands for Cu (II) complexes</b>
I) Oxamides	N, N'-bis(substituted) [131]
II) Pyrrolidine derivatives	Pyrrolidine dithiocarbamate [142]
III) Pyridine compounds	2,4-diiodo-6-(pyridine-2-ylmethylamino) methyl phenolate [143] 2,6-bis(benzimidazo-2-yl) pyridine (2-acetylpyridine) pyridine-2-carboxamidrazone [144] pyridylmethylbenzene-1,4-diamine [145]
IV) Benzimidazoles [146]	2,2-bipyridine/o-iodohippuric acid [147]
V) Chinolone derivatives	schiff base of benzimidazole [80]
VI) Pyrine analogs	N-propyl-Norfloracin and 1,10-phenanthroline [148] 6-(2-chlorobenzyl amino) purine [149] 6-(3-chlorobenzylamino) purine [149] aldehydes/2-amino-2-thiazoline [150]
VII) Schiff bases	vanillin-Schiff bases [151] L-Glycine/1,10-Phenanthroline [152] L-Tyrosine/salicylidene [153] L-Valine/1,10-phenanthroline [154]
VIII) Hydrazones [155]	benzaldoxime [157]; resorcyaldoxime [157]; salicyaldoxime [158]
IX) Thiosemicarbazones [156]	
X) Oximes	
XI) Mixed ligand Cu (II) Complexes	diimines/N,N-bis(benzimidazol-2-ylmethyl)amine [159] diimines/L-Tyrosine [160] hydroxyphenones/salicylaldehydes [161] 1,10 phenanthroline/bipyridine [153] 1,10-phenanthroline/imidazolidine-2-thione [162] 1,10-phenanthroline/Doxycycline [163] 1,10-phenanthroline/Tetracycline [163]

An important trend in the investigation of novel antineoplastic agents is the development of arene complexes, derivatives of Ferrocene, and scorpionates.

## CONCLUSION

The more pronounced different effects of metal complexes are combinations of anticancer and the following different activities: anti-Alzheimer, antioxidant, antimicrobial, antimalarial, anti-*Mycobacterium tuberculosis*, antifungal, anti-Leishmanial, antitrypanosomal, antiinflammatory, anti-rheumatic. Some metal-based complexes as Auranofin and Bortezomib have been approved as drugs.

### An important future trends include:

- 1) schiff base complexes of Co (II), Cu (II) [164,165]. Ni (II), Mn (II), and Cd (II) [165];
- 2) scorpionate complexes, such as of Cu(I) [166], Zn (II), Co (II) [167]. vanadium [168];
- 3) dinuclear complexes of Cu(I) [169];
- 4) mixed-ligand strategy [170];
- 5) Ruthenium (II) [171] arene complexes containing ligands, such as benzhydrazone [172]. isoquinoline [173]. Triazole [174], quinoxaline [175];
- 6) iridium(I) [176], osmium (II) [177]. palladium (II) [178].

An important perspective trend is the development of natural product-conjugated metal complexes for cancer therapy with ligands from plant origin as:

- 1) Ferrocene podophyllotoxin [179];
- 2) Ferrocene conjugates with flavonoids [180];
- 3) Ru (II) complexes with 18 $\beta$ -glycyrrhetic acid [86]; naphthoquinone/p-cymene [92];
- 4) Curcumin metal-based complexes [95].

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**Conflicts of interest:** The authors declare no conflict of interest.

**Author contributions:** All authors have contributed equal

### Ethical statements

- The authors declared that no clinical trials were used in the present study.
- The authors declared that no experiments on humans or human tissues were performed for the present study.
- The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

- The authors declared that no experiments on animals were performed for the present study.
- The authors declared that no commercially available immortalized human and animal cell lines were used in the present study

#### Data availability

All of the data that support the findings of this study are available in the main text or Supplementary.

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