

Processi, prodotti e servizi  
*Processes, products and services*

DII research group  
TCMET



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The research in the field has been started and successfully carried out by Prof. Rino Michelin, recently passed: it was our deepest privilege to have worked with him.

The research is ongoing and carried out in collaboration with Cristina Marzano and Valentina Gandin (Department of Pharmaceutical Sciences, UNIPD) as for the biological and cytotoxic activity, Alessandro Dolmella (DFS) as for X ray structural determinations and Alfonso Venzo (CNR) as for NMR characterization. Other relevant collaborations: Armando Pombeiro, IST, Lisbon and Tamas Kiss, University of Szeged (HU).

Main research topics:

- Design, synthesis and characterization of organometallic compounds of transition metals
- Design, synthesis and study of catalytic activity of new green catalytic systems
- Design, preparation and characterization of metal nanoparticles
- Preparation of nanocomposites with improved designed and tuned properties
- Supramolecular chemistry
- Supramolecular polymers
- Study of new approaches in environmental cleaning processes: application of photocatalysis
- Evaluation of chemical bases of technologies and proposal of innovative solutions

## Neutral and cationic platinum amidine and iminoether complexes: new classes of potential antitumor drugs

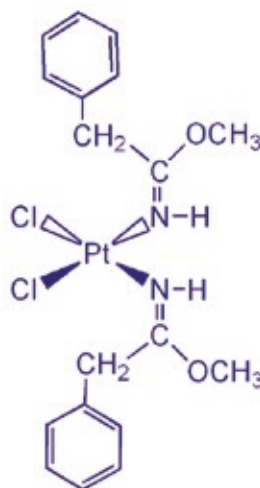
Platinum complexes are routinely used in clinical practice for the treatment of solid tumors. Unfortunately, the therapeutic outcome of platinum-based chemotherapy is massively impaired by severe side effects and intrinsic or acquired resistance.

Platinum amidine and iminoether complexes represent new classes of potential antitumor drugs which contain the imino moiety  $\text{HN}=\text{C}(\text{sp}^2)$  bonded to the platinum center.

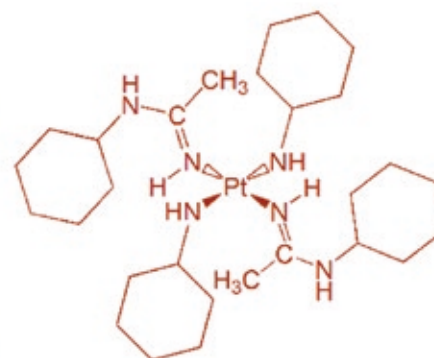
The iminoether complex *cis*- $[\text{PtCl}_2\{\text{E}-\text{N}(\text{H})=\text{C}(\text{OMe})\text{CH}_2\text{Ph}\}_2]$  (1) showed to be significantly more potent than cisplatin (the reference drug) against some tumor cell lines and able to overcome cisplatin resistance (Table 1).

*In vivo* studies on two transplantable tumor models (L1210 leukemia and Lewis lung carcinoma) showed that 1 induced a remarkable antitumor activity, as measured by prolonged survival and reduced tumor mass compared to control. The water soluble complex *trans*- $[\text{Pt}(\text{NH}_2\text{Cy})_2\{\text{N}(\text{H})=\text{C}(\text{NHCy})\text{CH}_3\}_2](\text{Cl})_2$ , (2) distinguished itself as the most promising derivative among a series of dicationic bis-amidine *trans*- $\text{Pt}^{\text{II}}$  complexes: using PEG400 as a solvent, it showed to be able to overcome both cisplatin and MDR resistance, inducing cancer cell death through p53-mediated apoptosis. *In vivo* studies on C57BC mice bearing Lewis lung carcinoma highlighted a significant and dose-dependent tumor growth inhibition without adverse side effects.

Complex 1



Complex 2



Complex	Hela	MCF-7	A375	A549	Caco-2	Hep-42	HL60
1	3.01±0.4	19.11±1.3	9.15±1.2	2.33±1.7	5.37±1.4	7.05±1.2	5.59±2.7
cisplatin	11.75±1.5	30.18±1.5	20.28±1.3	39.27±1.9	35.37±1.4	21.54±1.3	18.35±1.6
	2008	C13*	RH4	LoVo	LoVo MDR	A2780	A2780 ADR
2	6.30±2.06	5.22±1.45	13.24±2.05	11.01±2.43	15.02±1.58	9.43±2.52	9.35±1.53
cisplatin	12.69±1.73	89.18±1.54	26.76±1.75	1.43±0.20	44.87±3.13	1.91±1.54	27.32±1.61