Tentative Outline

Special Issue for Current Medicinal Chemistry

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Organometallic and Coordination Complexes: Rational design and fine-tuning of metalligand systems aimed at versatile application in Medicine

Aims & Scope:

In the past decades, the growing interest in organometallic and coordination compounds have been motivated by their remarkable structural diversity, potential applications in advanced materials and their relevance as structural and functional models for bioinorganic drugs and active sites of some metalloproteins and metalloenzymes.

Most of the medical treatments accepted by FDA for different diseases including mental and degenerative diseases are treated with antibodies and organic agents. Some of these organic molecules come from natural sources as flavonoids or alkaloids and on the other hand, some have been prepared by synthetic or semi-synthetic methods. Imatinib, placitaxel, topotecan, doxorrubicin are some of the antineoplastic drugs listed by health regulatory organizations such as WHO, OPS and NHI, while donepezil, galantamine and flavonoids derivatives stand out as reducing agents of emergence of behavioral disturbances and improvement in existing behavioral problems in patients with mild to moderate Alzheimer's.

A major problem of some pharmaceutical agents is its low aqueous solubility with consequent limited absorption and bioavailability. The structural richness of alkaloids, flavonoids and others heterocyclic compounds confer chelating abilities due to the presence of hydroxyl, amine and oxo groups that can have profound effects on their pharmacokinetic and pharmacological properties, among of them hydrophilic and bioavailability [1-3].

After the therapeutic potential of cisplatin discovery, there was explosive development of coordination chemistry, whose researchers have focused their efforts on synthesis, structure and cytotoxic effect of platinum (II) complexes with different ligands. However, the secondary effects have promoted the search to other metal ions and their complexes.

Organometallic and coordination compounds still offer a diverse platform of he rational design and fine-tuning of metal-ligand drug systems through their versatile geometries, coordination numbers, oxidation states that transform them into powerful therapeutic alternatives thanks to their antioxidant, proliferative inhibitors, antibacterial and antifungal properties [3].

Although to this day the exact mechanisms of action and biomolecular interactions have not been elucidated, the structural knowledge of the coordination compounds including the physicochemical properties from the tuning of the ligands by substitution or derivatization is crucial to allow more light on the structure-activity correlation towards biomolecular targets. Khater et al [1], discussed the ability of flavonoids to coordinate with metal atoms and how has provided new leads for drug discovery programs, with better pharmacological activities and clinical profiles than the parent flavonoids. The authors approximate the influence of hydroxyl substituents in the B ring as the main structural features responsible for the antioxidant activity of flavonoids. The 3´, 4´ ortho-di-hydroxyl groups form ortho-semiquinone

radicals that are highly stabilized by the electron delocalization and intramolecular hydrogen bonding. The combination of resonance of the aromatic C ring with C=O group in the central ring also assists in the delocalization of the π-electrons in ring B. This in turn influences the dissociation of phenolic hydroxyl groups as well as the stability of the formed phenoxy radicals in ring B. Additionally, the highest increase in activity is evidenced upon complexation of metals with flavonoids lacking the essential structural features of antioxidant activity such as chrysin, naringin, luteolin. For instance, complexation of vanadium metal with chrysin increased ABTS scavenging activity from 0.9 mM for chrysin to 3.96 mM. In this sense, possible mechanisms of action for the metal complexes, such as DNA binding and apoptosis induction, are also presented and the different techniques used for their characterization.

Malinowska et al. [4] described the medical applications of complexes of metal ions with small heterocyclic compounds containing nitrogen atoms within three-or five-membered rings. Such derivatives of pyrazoles, aziridines and diaziridines with metal ions like Cu(II), Zn(II) and Ru(III) exhibit interesting biological activity and their antioxidant, anticancer, anti-inflammatory, immunomodulatory and antimicrobial properties are presented. The authors have collected the results of the studies from the last years that concern antimicrobial and anticancer properties of pyrazoles complexes and the potential application of aziridine-containing natural compounds as chemotherapeutics with anticancer and antimicrobial agents. The article also pointed out the need for conducting more detailed pharmacological studies on these kinds of compounds as in vitro research seems to be interesting but also insufficient.

The aim of this issue is devoted to all aspects of synthetic strategies to obtain coordination compounds and their functionalizing for biomedical application such as antineoplastic, antiparasitic, antioxidant either the pharmacology direct action as drug delivery.

Subtopics:

- Studies of isolation, synthesis and chemical characterization of new potential drugs against chronic and neurodegenerative diseases
- Studies of structure-activity relationship and computational design to improve the current drugs and to propose novel drugs against neuro-degenerative diseases by using coordination compounds
- Clinical trials and medical applications of the active metal-ligand as natural and synthetic compounds

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