Diagonally Related Elements Ga, Sn and Bi in Pharmaceutical Applications

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Abstract

Metal complexes provide new opportunity for designing metal based pharmaceutical (metallodrug) industries with definite properties. The number of diseases and their treatment depend on the metabolism of inorganic constituents. The advancement in inorganic chemistry provides a golden opportunity to use metal complexes as therapeutic and diagnostic agents. The mode of action of metal complexes on living organism is different from non metals. The present article summarizes various pharmaceutical applications of some diagonally related trace metals (Ga, Sn, Bi) and their complexes.

Key words: Metal complexes, Ga, Sn, Bi, therapeutic and diagnostic agent.

1. Introduction

The use of metals and metalloids as pharmaceuticals has been known since antiquity. The common salt was used to cure many diseases at the time of ancient Greeks of Aesculapius and Hippocrates. Zn and Hg complexes found application in healing wounds. Arsenic, arsenicoxide (salvarsan) and diamino arsenobenzene were used to cure microbial infection[1].

Search for medical applications of inorganic compounds could lead to more discoveries in the field of coordination chemistry and organometallics. The interaction between metal complexes and biological molecules depends on the co-ordination properties, ligand exchange, photophysical and redox properties of metal ions[2]. The proliferation of modern medicinal chemistry with inorganic moiety reaches a dominating height with the discovery of a platinum compound, cis-platin by Rosenberg (1965), which has antibiotic and antitumor activity[3]. After a successful application of cis-platin and its analogs, various drugs have been prepared and used together with other metal and metalloid compounds[4]. Now, metal/metalloid elements such as bismuth, zinc, thallium, gallium, titanium, arsenic, antimony, selenium, gold, copper, vanadium, manganese, iron, ruthenium, etc. have found immense attention for designing important therapeutic drugs and diagnostic agents

Certain elements at trace concentrations have vital importance in medical applications. Gallium nitrate is a metallodrug that has clinical activity in the treatment of non-Hodgkin's lymphoma and urothelial malignancies[5-8]. Several clinical trials conducted over the past two decades as well as more recent studies conducted in patients with lymphoma have confirmed its antineoplastic activity when used as a single agent or in combination with other chemotherapeutic drugs. Tin is added to some dental care products as stannous fluoride (SnF_2) which is used as an anti-cavity ingredient in toothpastes and can be mixed with calcium abrasives while the more common sodium fluoride gradually becomes biologically inactive combined with calcium[9]. Certain Bi compounds like bismuth sub-carbonate and bismuth subnitrate are used in medicine. Bismuth subsalicylate is used as an antidiarrhoeal drug and to treat some other gastro-intestinal diseases. Bismuth thiols (BTs) are broad-spectrum anti-infectives with potent ability to overcome antibiotic resistant bacteria[10]. Also, an organic molecule containing Bi is used to treat eye infection [11].

A careful observation of periodic properties elements reveals that on moving across a period of the periodic table, the size of the atoms decrease, and on moving down a group the size of the atoms increase. Similarly, on moving across the period, the elements become progressively more covalent, less basic and more electronegative, whereas on moving down the group the elements become more ionic, more basic and less electronegative. Thus, on both descending a group and crossing by one element the changes "cancel" each other out. As a consequence diagonal members are often found to have similar atomic size,

electronegativity and similar properties of their compounds. Herein, we discuss the pharmaceutical applications of the three diagonally related elements Ga, Sn and Bi both in trace elemental concentration and as pharmaceutical formulations.

2. Pharmaceutical Application of Gallium

Gallium is a 13th group metal, having atomic number 31 and exist in liquid state at room temperature. Gallium has low absorption, no known physiologic function in the human body, the inert nature with cellular process and biologically important proteins, especially those of iron metabolism. This has led to the development of certain gallium compounds as diagnostic and therapeutic agents in medicine especially in the areas of metabolic bone disease, cancer, and infectious disease[12-13]. Some therauepic and diagonestic application of gallium compounds and complexes are summarized in table 1.

Gallium compounds	**Diseases investigated**	**Reference**
Gallium nitrate (Ganite).	Hypercalcemia, metabolic bone diseases, bladder cancer lymphoma,other cancers and microbial infections	[5-8]
Gallium maltolate	Hepatoma, lymphoma, microbial infections	[13]
G4544	Metabolic bone disease, Osteoporosis, skeletal metastas	[14]
Tris(8-quinolonato) Ga(III) KP46	Lung cancer,melanoma,other cancers.	[15,16]
Organometallic gallium compounds	Various malignant cell lines	[17]
^{67}Ga citrate	Widely used radiopharmaceutical for the clinical diagnosis of certain types of neoplasms.	[18,19]

Table 1: Pharmaceutical application of Gallium compounds.

3. Pharmaceutical Application of Tin

Tin is a 14th group element that has an association with mankind from the discovery of copper-tin alloy at the beginning of bronze-age. Tin and its compounds had a wide variety of applications in agriculture, catalysis, art and medicine. After the discovery of antitumor

activities of cis-platin, several research groups tried to investigate the possible medicinal (therapeutic) applications of other metal compounds or metal based orgametallics, organotin compounds were in the fore-front of these.

Name of compound	**Medical/therapeutic application**	**Reference**
Organotin compounds	Anti-tumour activity	[20,21]
Triorgano-tin carboxylate	Bactericides and fungicides	[20]
Diorganotin thiolates, of the general formula $(CH_3OCH_2CH_2OCH_2CH_2CH_2)2Sn(SR)_2$	Human sleeping sickness (anti-trypanocidal activity)	[22]
SnF_2	Dental hygiene to inhibit dental plaque formation owing to its apparent prophylactic therapeutic character.	[9,23]
Dichlorotin(IV) protoporphyrin IX	Kaposi' sarcoma, a highly visible tumour that is frequently seen in patients with HIV.	[24]

Table 2: Pharmaceutical application of Tin compounds.

4. Pharmaceutical Application of Bismuth

Bismuth is an element of 15^{th} group and has an atomic number 83. It is regarded as a heavy metal having two oxidation states (III/IV). Due to the high stability in aqueous solutions of bismuth derivatives with the oxidation number +3, it is regarded as the relevant bismuth species in biological system not bismuth derivatives with oxidation number (V). Bismuth is

seen as the least toxic heavy metal for humans and is widely used in medical field. This mini review describes few therapeutic and diagnostic applications of some bismuth compounds and its complexes.

Bismuth compounds	**Diseases investigated**	**Reference**
Ranitidine bismuthcitrate(RBC), Bismuthsubsalicylate(BSS) (Pepto Bismol),Bismuth sub citrate(BSC)	Gastric and Duodenal ulcer, Helicobacter pylori infection,	[25]
Bismuth thiol (BT)	A broad spectrum antibiotic, biofilms, chronic and acute wound infection, Biodefense (arthus, plagu etc), lungs infection, therapeutic pi lines.	[5]
Bismuth ethane dithio l(Bis-EDT)	*P. Aeruginosa*	[26]
Bismuth 2,3 dimercapto propanol(Bis-BAL)	*Klebsiella pneumoniae*	[27]
Bismuth containing cement materials for pulp capping	For dental infection	[28]
Colloidal bismuth subcitrate, (CBS), De-Nol®	Gastric and duodenal ulcer therapy	[29]

Table 3: Pharmaceutical application of Bismuth compounds.

5. Conclusion

With the advancement in medicinal chemistry, the role of metallodrugs as therapeutic and diagnostic agent is becoming increasingly important. A lot of gallium, tin and bismuth compounds have been investigated for potential bioactivity but few definitive interactions of

these with biological molecules have been reported. The metallodrugs are medically important for curing diseases but they may also have adverse effects on human body or living body due to overdosing.

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