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Review

Medicinal properties of organotin compounds and their limitations caused by toxicity

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ABSTRACT

Organotin(IV) compounds are used globally as stabilizers, catalyzers and biocidal agents. However, due to the increased focus on the application of organotin(IV) compounds in health care, their use will no longer be limited to industry and agriculture. Bioactivities of organotins including anti-cancer, antiviral, antiparasitic, antimicrobial, antihypertensive activities and anti-hyperbilirubinemia have been widely discussed and their anti-cancer abilities have been studied most extensively. Various series of organotins with different structural characteristics have been described including the diorganotin(IV) arylhydroxamates synthesized by our group. However, some factors, such as the high toxicity, have limited the application of organotins as drugs, despite their multiple biological activities. We reviewed and analyzed 829 cases of organotin(IV) poisoned patients in China, and found that organotins are the obvious risky factors of environmental contamination. The severe toxicities of organotin(IV) pollutants have been extensively investigated over the past few decades. Reproductive toxicity, neurotoxicity and other toxic effects can be caused by these compounds. Organotins with medicinal properties also exhibit the similar toxicities hampering their development as therapeutic agents. Therefore, it is important to discover more effective and safer medicinal organotins for therapeutic use by designing and synthetizing new organotin(IV) compounds.

Lin Niu was born in 1988 in Yangquan Shanxi Province of China, and studied pharmacy major at Shanxi Medical University since 2008. She is the student of Professor Qingshan Li and Professor Yunlan Li studying for a graduate degree now. Her major research interest is the toxicity mechanism research of organotin compounds, especialy the influence of cytochrome P450 by anticancer diorganotin compound DBDCT and its probable mechanism.

Abbreviations: PVC, polyvinyl chloride; TBT, tributyltin; DBT, dibutyltin; IC_{50}, half inhibitory concentration; MDR, multidrug resistance; Pgp, P-glycoprotein; PEG, polyethylene glycol; GI_{50}, growth inhibition 50%; ID_{50}, the half-inhibition dose; NSAIDs, non-steroidal antiinflammatory drugs; LOX, lipoxygenase; COX, cyclooxygenase; TB, tuberculosis; HSV, herpes simplex virus; TMT, trimethyltin; TTST, triphenyltin salicylanilide thiosemicarbazone; SOD, superoxide dismutase; EEG, electroencephalograph; ECG, electrocardiograph; DBDCT, di-*n*-butyl-(4-chlorobenzohydroxamato)tin(IV) chloride; DPDCT, di-phenyl-di-(2,4-dichlorobenzohydroxamato)tin.

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Dr. Qingshan Li, born in May, 1965, professor of Medicinal Chemistry, is an author of more than 260 papers on international and Chinese journals and author of 27 patents(two internationals). He is leading a research group in medicinal chemistry, drug pharmacokinetics and drug action mechanism. He maintains relationships with several research groups of Japan, Portugal and USA along with those of Peking University and other universities. He is the supervisor of 87 theses, the scientific coordinator of three projects from National Natural Science Foundation, coordinator of three projects from State Science and Technology Ministry, coordinator of two projects from State Education Ministry and coordinator of more than twenty projects from Shanxi Province. He is the winner of several important academic honors due to his achievements.

Contents

1. Introduction

Since the syntheses of organotin(IV) compounds were first reported by Frankland and Ann [1] in 1849, more researchers have focused on the synthesis and application of organotins. Generally, the organotin compounds, which are widely used in agricultural and industrial production, can be classified as heat stabilizers, catalysts and biocides. Mono- or di-substituted organotin(IV) compounds are usually added to the packing materials and pipes as stabilizers to attenuate the dehydrochlorination of chlorinated compounds, such as polyvinyl chloride (PVC) polymers, and to prevent oxygenolysis [2,3]. Owing to the low-energy 5-d orbitals of tin atoms, organotin(IV) catalysts are used in transesterification, esterification, and cross-linking reactions [3]. There are many advantages in the application of organotins such as high efficiency, small reaction amount, easy product separation and no corrosiveness for reactors. Organotin biocides are used as wood preservatives, molluscicides, acaricides, disinfectants, fungicides, insecticides and marine antifoulants [3,4]. However, the use of some organotin biocides has now been banned to different degrees in many areas to protect the environment.

In addition, more researches have been made on the application of organotin(IV) compounds in health care. These compounds have attracted attention not only because of their potential as anti-cancer drugs, but also because of their anti-inflammatory, anti-tuberculosis, anti-leishmaniasis and antibacterial activities.

In this article, we reported research results on the potential medicinal properties of organotin(IV) compounds for the applications described above. We also emphasized the importance of organotin(IV) toxicities which co-occur with the effective bioactivity and influence their medicinal value and use. It is necessary to improve the development of these compounds for medicinal applications while providing low-toxicity solutions.