International Journal of Progressive Sciences and Technologies (IJPSAT)
Vol. 2 No. 2 April. 2016, pp. 40-42

http://ijpsat.ijsht-journals.org

Boron Complexes as Anticancer Agents and Recent Advances

Ayodele Temidayo Odularu

Department of Chemistry, University of Fort Hare,
Private Bag X1314, Alice 5700, South Africa.

ABSTRACT: Outstanding ability of non toxicity of elemental boron is very relevant to health and it promotes green chemistry. The geometry of trigonal boron uses the empty p-orbital of boron to make it physiologically complianced to with nucleophiles to form boron complexes. These organoboranes are efficient anticancer agents. Presently, boron nanotubes with thermal neutron irradiation are possible candidates used as boron delivery vehicles for boron neutron capture (BNCT) chemotherapeutic agents. Research is still on to further develop the potentials of boron- containing- compounds as antitumour and anticancer agents.

KEYWORDS: Dry ashing, fenugreek, black cumin, ginger, garlic, atomic absorption spectrometry .

1. INTRODUCTION

1.1. HISTORICAL USE OF BORON AND ITS COMPOUNDS

About 6000 years ago, the Babylonians were familiar with compounds of boron, but there was a report that the Egyptians, Chinese, Tibetans and Arabians had used the compounds [1, 2]. In early nineteenth century in 1808, Sir Humphrey Davy, Joseph-Louis Gay-Lussac and Louis- Jaques Thénard discovered boron [2, 3]. The origin of the name was derived from the Arabic,"buraq", which was the name given to borax [2, 3]. They prepared boron by electrolysis of moistened boric acid and also from reduction of moistened boric acid, which both resulted to about 50% purity [1].

Fifty years after the discovery of boron, products of impure boron which were similar to diamond and graphite were synthesized [2]. Later, amorphous light boron of higher purity of about 90% was synthesized from reduction of boron trioxide with magnesium [4]. In the twentieth century, interest in boron increased due to their remarkable complex compounds [2]. Boron's reactive nature contributes to its occurrence in combined states, which include boracites ($Mg_7B_{10}Cl_2O_{30}$), colemanite ($Ca_2B_6O_{11}$), kernite ($Na_2B_4O_7 . 4H_2O$), sassolite (H_3BO_3) and ulexite ($CaNaB_5O_9 . 8H_2O$) [5].

The world's main source of boron is kernite ($Na_2B_4O_7 . 4H_2O$) from California, United States of America [1]. Boron has similar uses like glass due to its hard and brittle nature. Boron can be added to alloys, pure metals and solids to improve its strength. Aluminium dodecaboride (AlB_{12}) and boron carbide are used as substitutes for diamond dust for grinding and polishing [1].

Boron trifluoride is used for detecting gas tube neutron radiation, to examine radiation levels in space and in earth's atmosphere, industrial catalyst for organic reactions such as polymerization reactions and plays important function in the electroplating of lead, nickel and tin [2]. Borax is used in manufacturing heat-resistant borosilicate glass, having a trademark of "Pyrex" and a starting material for other boron compounds [1].

Corresponding Author: Ayodele Temidayo Odularu (ayodeleodularu@gmail.com)

2. Chemistry Of Boron And Its Compounds

Elemental boron is not toxic [2]. For trigonal boron, its geometry is trigonal planar and under some conditions form dative bond through its empty p-orbital with biological anions [6]. The utilization of this empty p-orbital expands the design of boron drugs, which makes them potent chemotherapeutic agents [8, 9]. Borax ($Na_2B_4O_7.10H_2O$), a combined form of boron had been used since early times as antiseptic and cleansing agents due to its properties of water-softening and detergent [1, 2]. Boron is applicable in synthetic chemistry due to its ability to react with carbon with covalent bonds [10]. Boric acid has properties of antifungal, antiseptic and antiviral properties; therefore, it is applicable as a mild antiseptic as eye washer and neutron absorber in the swimming pool [6]. High dosage (12.5-50 mM) of boric acid slows cell replication and caused induction of apoptosis in breast cancer cells (MD 231) and melanoma cells [7]. Boronic acids are effective and selective inhibitors of the mobility and feasibility of cancer cells [7]. Boromycin ($C_{45}H_{74}BNO_{15}$) is a potent anti-human immunodeficiency virus (HIV) antibiotic [6]. Boron based drug, such as benzoxaboroles had been stated as potential treatment for Chagas disease, malaria and trypanosomiasis. Bortezomib ($C_{19}H_{25}BN_4O_4$) has a trademark of Velcade, was the first FDA endorsed therapeutic drug for treating multiple resistant myeloma (cancer of plasma cells) and mantle cell lymphoma [6, 10-12]. The structure is shown in Figure 1. Boranes are useful for treating cancer and amino-carboxyboranes are potent cytotoxic and antineoplatic agents [7, 13]. Boromycin selectively disturbs cell cycles of cancer cells during G2, making them susceptible to anticancer agents [8]. They are also innate bacterial polyether-microcline because they possess antibiotic properties [8]. Presently, boron containing drugs are in the pharmaceutical stores and some are at different stages of clinical trials [8].

Trace concentration of boron helps in plant growth, while large concentration can be toxic [14]. Boron builds up in the body through absorption and ingestion [15]. The inhalation of boron compounds affects the central nervous system [2, 16]. Toxic effects are body rashes, circulation depression, coma, diarrhoea, shock and vomiting [17, 18].

Study revealed that insufficient boron in diet could be responsible for various types of cancer such as cancers of the breast cervix and prostate [19].

2.1. Boron Neutron Capture (BNCT)

In 2011, Scorei reported the necessity to find and develop boron-containing compounds as antitumour agents [19]. Prior to report of Scorei, Zhu et al in 1910 accounted for the main use of boron neutron capture (BNCT) to treat different forms of cancer [20]. Ortho carborances were adsorbed successfully on adapted magnetic nanoparticles through catalytic azide-alkyne cycloadditions [20]. Barry et al stated the exceptional properties of dicarbo-closo-dodecarboranes having high symmetry and unique stability which had led to wide applications [21]. They further stated the use of carborances as building blocks in some systems like dendrimers, polymers and nanoparticles. In order to develop boron containing drugs, carborances were studied as possible neutron capture (BNCT) chemotherapeutic agents and bioisosters of phenyl groups and pharmacophore [21]. Barry et al in 2014, reported the need for an efficient delivery of boron agents to overcome the challenge of clinical development [21]. In 2015, Nakamura et al were able to respond to Scrorel and Barry et al calls with the knowledge of their material chemistry [22]. They combined boron nitride nanotubes with thermal neutron irradiation as potential candidate as boron delivery vehicle for boron neutron capture (BNCT) chemotherapeutic agent [22].

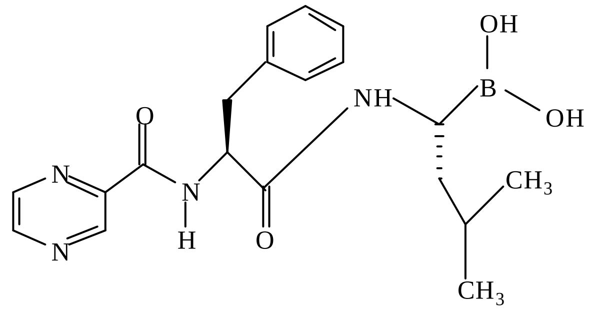

Fig. 1. Structure of Bortezomib

3. CONCLUSION

The non-toxic nature of boron and low cost has made it to be considered for versatile applications. Ligands could coordinate with the empty p shell of boron which enables it to form organoboranes, most applicable in drug discovery, design and development. The present use of boron neutron capture (BNCT) is essential for drug delivery. Further studies are on to improve on the present clinical stage.

References

[1] J. Wisniak, "Borax, Boric acid and Boron-from Exotic to Commodity," Industrial Journal of Chemical Technology, vol. 12, pp. 488-500, 2005.

[2] Boron, [Online] Available: http://nautilus.fis.uc.pt/st2.5/scenes-e/elem/e00500.html (December 28, 2015)

[3] Stewart Doug, Discovery of Boron; Boron Element Facts, [Online] Available: http://www.chemicool.com/elements/boron.html. (December 28, 2015).

[4] M. Vignolo, G. Romano, C. Bernini, A. Martinelli and A. S. Siri, "A Novel Process to Produce Amorphous Nano-Sized B Useful for MgB2 Phase Synthesis," IEEE Transactions on Applied Superconductivity, vol 22, no 4, pp. 1-16, 2014.

[5] D. Schubert, "Boron Oxides, Boric Acid and Borates," Kirk-Othmer Encyclopedia of Chemical Technology, 2011.

[6] B. S. Sekhon,"Metalloids Compounds as Drugs," Research in Pharmaceutical Sciences, vol. 8, no 3, pp. 145-158, 2013.

[7] R. I. Scorei and R. Popa, "Boron-Containing Compounds as Preventive and Chemotherapeutic Agents for Cancer," Anti-Cancer Agents in Medicinal Chemistry, vol. 10, no. 4, pp. 346-351, 2010.

[8] S. J. Baker, C. Z. Ding, T. Akama, Y. Zhang, V. Hernandez and Y. Xia, "Therapeutic Potential of Boron-Containing Compounds. Future Medicinal Chemistry, vol. 1, no 7. pp 1275-1788, 2009.

[9] B. S. Burnham, "Amines-Boranes," Metalloproteins Encyclopedia, 2013.

[10] B. C. Das, P. Thapa, R. Karki, C. Schinke, S. Das, S. K. Banerjee, P. V. Veldhuizen, A. Verma, L. M. Weiss and T. Evans, "Boron Chemicals in Diagnosis and Therapeutics," Future Medicinal Chemistry, vol. 5, no. 6, pp. 653-676, 2013.

[11] D. Steverding and X. Wang, "Trypanocidal activity of the Proteasome Inhibitor and Anti-Cancer Drug Bortezomib," Parasites and Vectors, vol. 2, no. 29, pp. 1-4, 2009.

[12] S. B. Aeschbacher, D. Huber, C. Spiliotis, M.; Müller and A. Hemphill, "Profound Activity of the Anti-Cancer Drug Bortezomib against Echinococcus multilocaris Metacestodes Identifies the Proteasome as a Novel Drug Target for Cestodes," PLOS Neglected Tropical Disease, vol. 8, no. 12, pp. 1-13, 2014.

[13] B. S. Burnham, "Synthesis and Pharmacological Activities of Amines-Boranes". Current Medicinal Chemistry, vol. 12, no. 17, pp. 1995-2010, 2005.

[14] J. Morrissey and M. L. Guerinot, "Trace Elements: Too Little or Too Much and How Plants Cope," F1000 Biology Reports, vol. 1, no. 14, pp. 1-4, 2009.

[15] P. D. Howe, "A Review of Boron Effects in the Environment," Biological Trace Element Research, vol. 66, no. 1-3, pp. 153-166, 1998.

[16] S. Bakirdere, S. Örenay and M. Korkmaz, "Effect of Boron on Human Health," The Open Mineral Processing Journal, vol. 3, pp. 54-59, 2010.

[17] F. J. Murray, "A Human Health Risk Assessment of Boron (Boric Acid and Borax) in Drinking Water," Regulatory. Toxicology. Pharmacology: RTP, vol. 22, no. 3, pp. 221-230, 1995.

[18] B. D. Culver and S. A. Hubbard, "Inorganic Boron Health Effects in Humans: An Aid to Risk Assessment and Clinical Judgment" The Journal of Trace Elements in Experimental Medicine, vol. 9, no. 4, pp. 175-184, 1996.

[19] I.R. Scorei, "Boron Compounds in the Breast Cancer Cells Chemoprevention and Chemotherapy," pp. 91-114, 2011.

[20] Y. Zhu, Y. Lin, Y. Z. Zhu, J. Lu, J. A. Maguire and N. S. Hosmanes, "Boron Drug Delivery via Encapsulated Nanocomposites: A New Approach for BNCT in Cancer Treatment, Journal of Nanomaterials," vol. 2010, pp. 1-8, 2010.

[21] N. P. E. Barry, A. Pitto-Barry, I. Romero-Canel'on, J. Tran J. J, Soldevila-Barreda, I. Hands-Portman, C. J. Smith, N. Kirby, A P. Dove, R. K. O'Relly and P. J. Sadler, " Precious Metal Carborane Polymer Nanoparticles: Characterisation of Micellar Formulations and Anticancer Activity," Faraday Discussions, vol. 175, pp. 229-240, 2014.

[22] H. Nakamura, H. Koganei, T. Miyoshi, Y. Sakurai, K. Ono and M. Suzuki, "Antitumor Effect of Boron Nitride Nanotubes in Combination with Thermal Neutron Irradiation on BNCT," Bioorganic and Medicinal Chemistry Letters, vol. 25, no. 2, pp.172-174, 2014.