

Development of Metallodrugs Based on Bioelementology

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Since ancient time, metalloelements have been empirically used to treat diseases. Through the time of alchemy, Paracelsus (1493-1541) tried to use metalloelements for treating diseases to overcome the humor-physiology established by Galenus (130-201). The concept for medicinal chemistry proposed by Paracelsus created several kinds of classical metallodrugs such as antisyphilitic containing As, antidiuretic containing Hg, and antischistosomiasis containing Sb, and later in the 20th century produced new types of metallodrugs involving antipernicious anemia agents containing Fe and Co, antineoplastic agent containing Pt, antirheumatic containing Au, antiulcer agents containing Al and Zn, ischemia-reperfusion suppressor containing Se, antidepressant containing Li, and diagnostic and therapeutic radiopharmaceutic containing ^{99m}Tc . Such research field for developing metallodrugs is proposed as Bioelementology. As a part of endeavor to find possibility for developing new types of metallodrugs, a new progress of the research for aiming at the treatment of diabetes mellitus, which is considered to be one of the most important diseases in the 21st century in all over the world, will be introduced. Since our first finding of orally active vanadyl-cysteinmethyl ester complex to treat type 1 diabetic model animals in 1990, we have developed many kinds of vanadyl-containing complexes with different coordination structures by using the comprehensive research system consisting of synthesis, *in vitro* and *in vivo* evaluations in type 1 and 2 diabetic animals, pharmacokinetic feature and formulation of the complexes. The action mode of the complexes was named as “ensemble mechanism”. Future perspective is also discussed.