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Review

Vanadium compounds in medicine

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ABSTRACT

Vanadium is a transition metal that, being ubiquitously distributed in soil, crude oil, water and air, also found roles in biological systems and is an essential element in most living beings. There are also several groups of organisms which accumulate vanadium, employing it in their biological processes. Vanadium being a biological relevant element, it is not surprising that many vanadium based therapeutic drugs have been proposed for the treatment of several types of diseases. Namely, vanadium compounds, in particular organic derivatives, have been proposed for the treatment of diabetes, of cancer and of diseases caused by parasites. In this work we review the medicinal applications proposed for vanadium compounds with particular emphasis on the more recent publications. In cells, partly due to the similarity of vanadate and phosphate, vanadium compounds activate numerous signaling pathways and transcription factors; this by itself potentiates application of vanadium-based therapeutics. Nevertheless, this non-specific bio-activity may also introduce several deleterious side effects as in addition, due to Fenton's type reactions or of the reaction with atmospheric O_2, VCs may also generate reactive oxygen species, thereby introducing oxidative stress with consequences presently not well evaluated, particularly for long-term

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administration of vanadium to humans. Notwithstanding, the potential of vanadium compounds to treat type 2 diabetes is still an open question and therapies using vanadium compounds for *e.g.* antitumor and anti-parasitic related diseases remain promising.

1. Introduction

Progress in the chemistry of vanadium, namely in the search of its therapeutic applications has been exponential during the last 10–15 years, and several reviews have been published, a few of them during the last five years [1–13], as well as a few others in distinct areas, not so well covered in the more recent reviews [14–20]. In this work we will make a review on medical applications of vanadium complexes, not trying to systematically cover all publications, but to make a more comprehensive text. The recent book edited by Michibata [20] includes chapters of 'Vanadium Effects on Bone Metabolism', 'Vanadium in Cancer Prevention', Cardiovascular Protection with Vanadium Compounds' and 'Inhalation Toxicity of Vanadium', thus these topics will only be shortly addressed.

1.1. Distribution, essentiality and potential toxicity of vanadium

Considering relative elemental abundance in our planet's crust, vanadium (0.019%) is the 18th element, thus not far from that of zinc (0.008%) [6]. It is ubiquitously distributed in soil, fossils (particularly in crude oil), water, air and living organisms. In sea water vanadium exists mainly in the form of $H_2VO_4^-$ and is the 2nd most abundant transition element, being about two orders of magnitude more abundant than iron [6]. The usual V concentrations in drinking water are in the 10 nM range, but groundwater from volcanic areas may contain much higher amounts, up to *ca.* 2.5 μM [6], and contamination is frequently observed in rivers, lakes and seas ([11] and references therein).

Many metal ions have a general tendency to interact with biomolecules, therefore, it is not surprising that natural evolution has incorporated many of them into performing a wide variety of tasks and playing crucial roles in living beings. Since nature has made such extensive use of metal ions, the questions: "*Can metal ions be incorporated into drugs? And can coordination chemistry be used with advantage for medicinal purposes?*" naturally arise and are the subject of Medicinal Inorganic Chemistry [7,21]. Vanadium, being ubiquitously present in our planet's crust also found roles in biological systems, and this work focuses on the potential uses of vanadium-based therapeutic compounds in Medicine.

Several groups of organisms accumulate vanadium and/or employ vanadium in life processes. On the basis of its high amount found in the earth' crust, namely in pre-biotic conditions and when life first appeared, and of its known use in biochemistry, vanadium is likely to have an essential role in most if not all living beings, namely in humans [2,6]. The average vanadium concentration in the human body is approximately 0.3 μM and with equilibrium between the amount excreted from the body and the constant supply of some vanadium *via* food and drinking water may easily be maintained [22].

The main routes of vanadium uptake and distribution in the human body are sketched in Fig. 1 (adapted from [6]). Non-occupational vanadium exposure is predominantly from the food supply and typical daily doses consumed by humans have been estimated at 0.01–0.03 mg V/day [5]. Dietary uptake is a quite ineffective process because most of the dietary vanadium is usually excreted with the feces (see below).

The main natural sources for vanadium loads in the atmosphere are continental dust evolving from weathering of soils, marine aerosols and volcanic emissions [11,23,24]. Other major sources for aerial contamination are from mining, industrial enterprises and burning of crude oil. In non-polluted areas, the concentration of vanadium oxides (VOx) is in the range of 50 ng m^{-3}, but pollution,

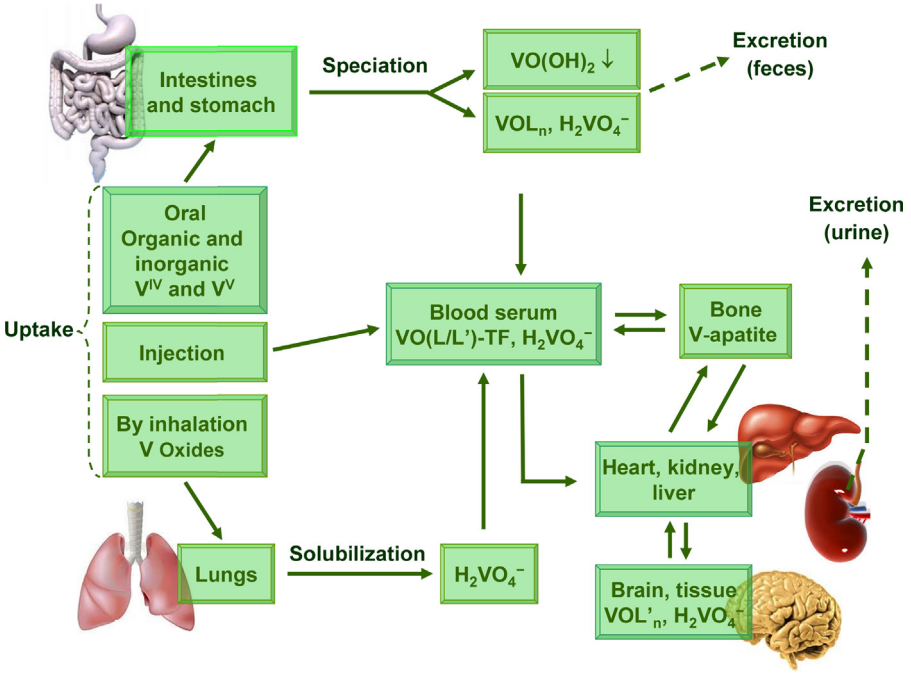

Fig. 1. Uptake and distribution of vanadium compounds in the body.

Source: Adapted from Ref. [6].