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Borates and their biological applications

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Abstract

This paper reviews some of the many biological applications of borates. Boron is a ubiquitous element found widely distributed in the environment and is a normal component of a healthy diet. Elemental boron does not exist in nature, but is always found combined with oxygen in compounds called borates. Boron is an essential micro-nutrient for plants, and there is evidence to suggest that boron is of nutritional importance, if not essential, for humans. Borates possess biostatic activity which enabled their use in medicine and has allowed their continued development as preservatives.

The essentiality of boron in plants has led to extensive biological use in agriculture. The biostatic properties at high doses have enabled their use in biodeterioration control, against insects, fungi, algae and bacteria. Some use is currently being made of borates for insect control in the home.

The application of borates to crops, to alleviate boron deficiency, has resulted in recognized increases in quality and yield. Consideration of the relative safety and effectiveness of borates as biocides, is expected to lead to an increase in the use of these products in the future.

Key Words: Applications; Biochemistry; Biology; Borates; Boron; Chemistry; Micronutrient; Preservative.

Introduction

The objective of this paper is to review some of the large scale commercial applications of boron which interact with biological systems. The relevant chemistry and biochemical interactions, which render borates bioactive molecules, are introduced. Boron chemistry and biochemistry is of particular interest as all of its physiological effects are as a direct result, even though some appear at first to be contradictory.

The two most well known which will be discussed in detail here are the essentiality of borates on the one hand and their toxicity or effectiveness as a preservative on the other. This is perhaps not such a surprise when one considers the ubiquitous nature of borates and the ability of most micro-nutrients to become detrimental at high physiological concentrations.

Boron is a trivalent element widely distributed in the environment, comprising about 0.001% of the earth's crust (The Merck Index, 1989); concentrations average 3-10 $\mu\text{g/g}$ in soil (Adams, 1964; Muetterties, 1967), 4.5 $\mu\text{g/g}$ in ocean waters (Weast, 1983), and about 0.01 $\mu\text{g/g}$ in freshwater (Jenkins, 1980).

Boron is widely distributed in plant and animal tissues and is known to be essential for plant growth (Gouch & Dugger, 1954; Skok, 1958; Skol'nik, 1974; Underwood, 1977; Lovatt & Dugger, 1984). In a review on its toxicity by Murray (1995), it was reported that: the average U.S. daily dietary intake of boron is 1.5 mg B/day. The median

(EPA, 1994) and the daily boron intake for humans from food and water has been estimated at 0.5 - 3.1 mg for adults (Nielson, 1992).

Chemistry of Boron

Boron is the only non-metal in a family otherwise comprised of active metals, group IIIb of the periodic table. As could be expected, boron exhibits bonding and structural characteristics intermediate to both, as do other elements lying to either side of the metal/non-metal border. Boron (Atomic number 5) also has a tendency to form double bonds and macromolecules, although these bonds are more correctly described as partial double bonds and are due to π electron back bonding into the empty p orbital of boron.

Because of an incomplete electron octet, boron compounds can act as electron pair acceptors and this behavior is demonstrated by the Lewis acid properties of boron. It is this tendency which is fundamental when forming hypotheses attempting to predict the action of boron within biological systems, as will be discussed.

Boron does not occur in nature in its elemental form, but rather as oxygen containing compounds such as boric acid ($B(OH)_3$), in some volcanic spring waters and elsewhere, as borates such as borax. These compounds are used as commercial products and for the synthesis of other boron compounds. In this paper and elsewhere, references to boron in the environment and in various applications, have referred to the elemental boron content, which in some cases allows for comparisons between studies and applications.

Oxygen containing compounds of boron are among the most important, comprising nearly all the naturally occurring forms. The structures of these compounds consist mainly of trigonal BO_3 units with sp^2 hybridization, and with tetrahedral BO_4 units with sp^3 hybridization (Cotton *et al.*, 1987). B-O bond energies are 560 - 790 kJ, with the only competition in strength offered by the B-F bond in BF_3 (640 kJ) (Cotton & Wilkinson, 1986). Endless organic derivatives containing boron-oxygen bonds are known; the main examples that include trigonal boron are the orthoborates ($B(OR)_3$ e.g. esters; the acyl borates ($B(OCOR)_3$); the peroxy borates ($B(OOR)_3$); and the boronic acids ($RB(OH)_2$). It is appropriate to consider that these are derivatives of boric acid (Cotton *et al.*, 1987).

Boric acid is a colorless, odorless, transparent crystals or as white granular powder (Anon, 1980). It is readily soluble in water, ethanol and glycerol (Merck Index, 1989). Borax is a white crystalline substance and is soluble in water and glycerol, but insoluble in alcohol (Merck Index, 1989). Three other sodium borates are commonly known: sodium metaborate ($NaBO_2$); sodium perborate ($NaBO_3 \cdot 4H_2O$); and sodium pentaborate ($Na_2B_{10}O_{16} \cdot 10H_2O$). Like boric acid and borax, they are soluble in water and glycerol (*ibid.*).

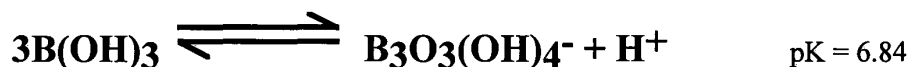
It is these oxygen containing compounds of boron that are traditionally used in biological applications. Boric acid, borax, mixtures of the two or a spray dried mixture equating roughly to disodium octaborate tetrahydrate, being the most commonly used, although organic esters of boric acid such as trihexylene glycol diborate, are also currently in use and boronic acids are used in minor applications. Perborates, boric acid

1980; Merck, 1989) and in fact boric acid was used as an antiseptic by Sir Joseph Lister, the father of modern surgery, in the mid 19th century.

Boric acid is moderately soluble in water, but has a large negative heat of solution so that the solubility increases markedly with temperature. It is a very weak and exclusively monobasic acid that is believed to act, not as a proton donor, but as a Lewis acid, accepting OH⁻:



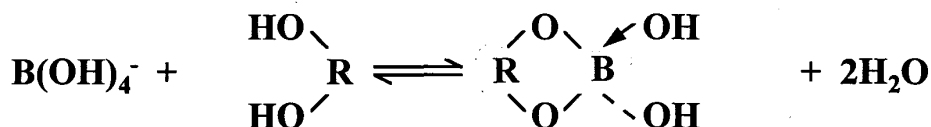
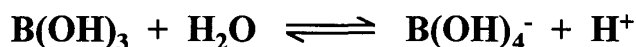
The B(OH)₄⁻ ion actually occurs in some minerals. At concentrations less than 0.025M, only the mononuclear species B(OH)₃ and B(OH)₄⁻ exist; but at higher concentrations the pH becomes consistent with the formation of polymeric species such as:



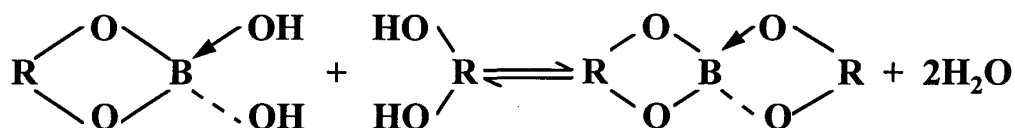
It is also likely that polymers exist in mixed solutions of boric acid and borates, such as:



Boron (in the form of boric acid or more probably ionized as the tetrahydroxy borate anion), is one of the chemical elements whose oxygen compounds will form chelate complexes with certain organic compounds containing *cis* adjacent alcohol groups:



and



These complexes occur in aqueous solution and are well known. Biot as early as 1842, reported that a solution of boric acid became acidic to litmus upon the addition of sugars and Thompson (1893) found that boric acid could be determined by titration in the presence of various polyhydroxy compounds (or polyols).

Many chemical and most biochemical reactions of boron are based on the reactivity of the borate anion with adjacent alcohol groups. These stable complexes formed by rapid esterification with polyols (Nickerson, 1970; Boeseken, 1949), are mainly 1 : 1 and charged. It has also been suggested that similar reactions take place with α -hydroxy carboxylic acids (Kustin & Pizer, 1969) and although this is true of gluconate for example, it has been shown that the complex is only formed as a result of an additional hydroxyl group in the β position as other α -hydroxy carboxylic acids such as lactate do not undergo the same reaction (Lloyd, 1993). The type of complexes formed with polyols depends on pH and on the ratio of the borate ion to the diol (Zittle, 1951) and the acidity of the hydroxy groups. When a low diol to borate ratio exists, it has been proposed that the monoester is prevalent, whilst when the diol to borate ratio is high, then the diester is predominant. The acidity of boric acid is thereby increased as mentioned above. Steric considerations are critical in the formation of these complexes. Thus 1,2- and 1,3-diols in the *cis*-form only, such as *cis*-1,2-cyclopentanediol are active, and only *o*-quinols react. Indeed the ability of a diol to affect the acidity of boric acid is a useful criterion of the configuration where *cis-trans*-isomers are possible.

This specific complex forming ability has led to the use of boric acid in carbohydrate separation and in determining carbohydrate configuration (Boeseken, 1949; Annison *et al.*, 1951; Khym & Zill, 1951; 1952; Popiel, 1961).

Biochemical Effects of Boron

Several compounds of biological importance such as vitamins and co-enzymes can react to form complexes with the borate ion (Zittle, 1951; Aruga, 1985). Reactions with these molecules and others within the cell, have been found to produce dramatic changes in metabolism.

A good example of this is the effect of boron on plant metabolism and lignification. Here the borate seems to play at least one role by partitioning metabolism between the pentose phosphate shunt and glycolytic pathways. Boron deficiency has been shown to result in an accumulation of phenolic compounds in plants (Dugger, 1983; Shkol'nik, 1974). An increase in lignification has also been observed under these conditions (Acerbo *et al.*, 1973). Such metabolic changes appear to be caused by a lack of the inhibition of glucose-6-phosphate and 6-phosphogluconate dehydrogenases, which are normally inhibited in the presence of boron. This inhibition in the case of 6-phosphogluconate dehydrogenase was suggested to result from the formation of a complex with boric acid and the α -hydroxy carboxylic acid, 6-phosphogluconate (Lee & Aronoff, 1967) but has been subsequently shown to be as a result of chelate formation with the co-enzyme NADP⁺ which also features in the reaction (Lloyd *et al.*, 1990; Lloyd & Dickinson, 1991; Lloyd, 1993). In the absence of boron, the pentose phosphate pathway is left unregulated and results in an over-production of phenolic acids and other lignin components. The accumulation of such compounds would not only lead to the necrosis of plant tissue, but also to an increased deficiency problem, as

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