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Diquat in Drinking-water

Background document for development of
WHO *Guidelines for Drinking-water Quality*

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Preface

Access to safe drinking-water is essential to health, a basic human right and a component of effective policy for health protection. A major World Health Organization (WHO) function to support access to safe drinking-water is the responsibility "to propose ... regulations, and to make recommendations with respect to international health matters ...", including those related to drinking-water safety and management.

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as *International Standards for Drinking-water*. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO *Guidelines for Drinking-water Quality* (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002. The third edition of the GDWQ was published in 2004, the first addendum to the third edition was published in 2006 and the second addendum to the third edition was published in 2008. The fourth edition was published in 2011, and the first addendum to the fourth edition was published in 2017.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of drinking-water quality is accordingly prepared and updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants of potential health concern in drinking-water. In the first and second editions, these constituted Volume 2 of the GDWQ. Since publication of the third edition, they comprise a series of free-standing monographs, including this one.

For each chemical contaminant or substance considered, a background document evaluating the risks for human health from exposure to the particular chemical in drinking-water was prepared. The draft health criteria document was submitted to a number of scientific institutions and selected experts for peer review. The draft document was also released to the public domain for comment. Comments were carefully considered and addressed as appropriate, taking into consideration the processes outlined in the *Policies and Procedures Used in Updating the WHO Guidelines for Drinking-water Quality* (http://apps.who.int/iris/bitstream/10665/70050/1/WHO_HSE_WSH_09.05_eng.pdf) and the *WHO Handbook for Guideline Development* (http://www.who.int/publications/guidelines/handbook_2nd_ed.pdf), and the revised draft was submitted for final evaluation at expert consultations.

During the preparation of background documents and at expert consultations, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Meeting on Pesticide Residues and the Joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite, in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO website and in the current edition of the GDWQ.

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Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document and in particular those who provided peer or public domain review comments are greatly appreciated.

Abbreviations

ADI	acceptable daily intake
ARfD	acute reference dose
bw	body weight
CAS	Chemical Abstracts Service
FAO	Food and Agriculture Organization of the United Nations
HBV	health-based value
ISO	International Organization for Standardization
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
K_{oc}	soil adsorption coefficient
K_{ow}	octanol–water partition coefficient
LD_{50}	median lethal dose
NOAEL	no-observed-adverse-effect level
WHO	World Health Organization
WHOPES	World Health Organization Pesticide Evaluation Scheme

Contents

Diquat is the International Organization for Standardization (ISO)–approved common name for 6,7-dihydrodipyrido[1,2-a:2′,1′-c]pyrazinediium dibromide, for which the Chemical Abstracts Service (CAS) number is 85–00–7. The CAS number for diquat ion is 2764–72–9 (WHO, 2014).

1. MAJOR USES

Diquat is usually formulated as an aqueous solution (FAO, 1995) or a compound product mixed with the herbicide paraquat (MacBean, 2012). It is a nonselective, quick-acting contact herbicide that produces desiccation (causing the leaf or the entire plant to dry out quickly) and defoliation by causing injury only to the parts of the plant to which it is applied (WHO, 2014). Diquat is used for weed control on several food crops, including potato and rice. It may also be used to defoliate seed or root crops for preharvest desiccation. Diquat has a number of outdoor residential weed control applications on lawns and ornamental plants, and it can also be used on paved areas and patios (USEPA, 2002). It may be used as an aquatic herbicide for the control of free-floating and submerged aquatic weeds in ponds and irrigation ditches (FAO, 1995).

2. POTENTIAL FOR OCCURRENCE IN WATER

Diquat is not taken up by plant roots and is not metabolically degraded by plants (FAO, 1995). It is highly soluble in water (718 g/L for diquat dibromide; Royal Society of Chemistry, 1988; FAO, 1995), and its octanol–water partition coefficient is very low (log K_{ow} −4.6 at 20 °C for diquat dibromide; FAO, 1995; MacBean, 2012). However, diquat is strongly adsorbed to soil; soil adsorption coefficient (K_{oc}) values (32 soils) ranged from 32 000 to 7 900 000 in a study in Denmark (European Commission, 2001). Diquat in the sorbed state is resistant to degradation, with a half-life ranging from 1.2 to 41 years (MacBean, 2012). In contrast, photochemical degradation in soil, as well as water, occurs in the presence of sunlight (FAO, 1995). Diquat photodegrades in the surface layer of water in 1–3 weeks or more when not adsorbed to particulate matter (USEPA, undated). When diquat is added to surface waters, residues in the water rapidly decline principally by adsorption to plants and then to sediments. Half-lives of diquat in natural waters are generally less than 48 hours (FAO, 1995).

Diquat was detected in water from marsh areas in Spain at an average concentration (which includes concentrations of 0 µg/L assigned to samples in which no diquat was detected) of 0.01 µg/L and a maximum concentration of 3.1 µg/L (Fernández et al., 1998). No diquat was detected (limit of detection 1 µg/L) in surface water in Japan from areas where significant quantities were used (Japan Water Works Association, 2009–2012).

3. TOXICITY

The Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Meeting on Pesticide Residues (JMPR) evaluated diquat in 2013 (FAO/WHO, 2014; WHO, 2014). The eye was the main target organ following short-term repeated exposure in rats and dogs. Effects on kidney, liver and haematological parameters were also observed. Diquat was not carcinogenic in mice or rats. In tests for genotoxicity, it gave an equivocal response in the absence of metabolic activation and a positive response in the presence of metabolic activation in the mammalian cell cytogenetic assay, but was negative in the in vivo mouse micronucleus assay and dominant lethal assay. No reproductive effects were observed at the highest dose tested in a two-generation reproductive toxicity study in rats, and diquat was not teratogenic in rats or rabbits.

JMPR (WHO, 2014) established an acceptable daily intake (ADI) of 0–0.006 mg/kg body weight (bw) (expressed as the diquat ion) from a no-observed-adverse-effect level (NOAEL) of 0.58 mg/kg bw per day (as the diquat ion) on the basis of cataracts seen at 2.9 mg/kg bw per day (as the diquat ion) in a 2-year toxicity and carcinogenicity study in rats (Colley et al., 1985). A safety factor of 100 was applied. This ADI was based on the same study and end-point selected by the 1993 JMPR (WHO, 1994), but using a different NOAEL (Harling, Buist & Gopinath, 1997a,b). The ADI was supported by a NOAEL of 0.53 mg/kg bw per day (as the diquat ion) based on cataracts seen at 2.53 mg/kg bw per day (as the diquat ion) in a 1-year toxicity study in dogs (Hopkins, 1990).

An acute reference dose (ARfD)[1] of 0.8 mg/kg bw was established by JMPR (WHO, 2014) on the basis of a NOAEL of 75 mg/kg bw (expressed as the diquat ion) in a neurotoxicity study in rats, based on clinical signs and decreased body weight gains in the first week and decreased feed consumption seen at 150 mg/kg bw (as the diquat ion) (Horner, 1992). A safety factor of 100 was applied. This ARfD was supported by an acute oral toxicity study in rats (median lethal dose [LD_{50}] of 214 mg/kg bw) in which no mortality or clinical signs of toxicity were observed at 100 mg/kg bw (McCall & Robinson, 1990). JMPR concluded that the critical effects in the longer-term studies of eye lesions were not likely to be produced following a single dose, as the eye lesions were normally evident only after several weeks of continuous dosing in the diet (WHO, 2014).

4. DERIVATION OF A HEALTH-BASED VALUE[2]

Pesticides provide a special case for establishing health-based values (HBVs) for drinking-water in terms of the potential exposure from other sources, because they are deliberately applied to food crops. JMPR concluded that the daily intake of diquat in food was up to 4% of the upper bound of the ADI (FAO/WHO, 2014), which suggests that exposure from food is low.

With an allocation of 20% of the upper bound of the unrounded JMPR ADI of 0.0058 mg/kg bw (expressed as the diquat ion) to drinking-water and the assumption that a 60 kg person consumes 2 L of drinking-water per day, an HBV of 0.03 mg/L (30 µg/L) can be derived for diquat (as the diquat ion). The default allocation factor of 20% has been used to account for the fact that available food exposure data, which suggest that exposure via this route is low, do not generally include information from developing countries, where exposure via this route may be higher (for further information, see Section 8.2.2, “Relative source allocation”, of the *Guidelines for Drinking-water Quality*; WHO, 2017).

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[1] The estimate of the amount of a substance in food or drinking-water, expressed on a body weight basis, that can be ingested in a period of 24 hours or less without appreciable health risk to the consumer.

[2] Formal guideline values are established when one of the following criteria has been met: 1) there is credible evidence of occurrence of the chemical in drinking-water combined with evidence of actual or potential toxicity, 2) the chemical is of significant international concern or 3) the chemical is being considered for inclusion or is included in the World Health Organization Pesticide Evaluation Scheme (WHOPES). For some chemicals, no formal guideline values are established when occurrence is likely to be well below a level that would be of concern for health. Establishing a formal guideline value for such substances may encourage Member States to incorporate a value into their national standards when this may be unnecessary. When a formal guideline value is not established, a “health-based value” may be determined in order to provide guidance to Member States when there is reason for local concern. This reference value provides both a means of judging the margin of safety in the absence of a specific guideline value and a level of interest for establishing analytical methods.

5. CONSIDERATIONS IN APPLYING THE HEALTH-BASED VALUE

The HBV for diquat is protective against health effects resulting from lifetime exposure to diquat from drinking-water. Small exceedances above the HBV for a short period are unlikely to have an impact on health. If these exceedances are due to massive contamination, however, such as that found in emergency or spill situations, an acute HBV of 20 mg/L (derived from the unrounded JMPR ARfD) would provide a useful point of reference for the provision of advice to consumers. This acute HBV indicates the concentration of diquat in drinking-water that a person could consume for 24 hours without appreciable health risk (for further information, see Section 8.7.5 of the *Guidelines for Drinking-water Quality*; WHO, 2017).

Routine monitoring of diquat is not considered necessary. However, Member States should consider local usage and potential situations such as spills in deciding whether and where to monitor. In the event that monitoring results show levels above the HBV on a regular basis, it is advisable that a plan be developed and implemented to address the situation.

As a general principle, efforts should be made to keep the concentration of pesticides in water as low as possible and to not allow concentrations to increase up to the HBV.

6. ANALYSIS IN WATER

Analytical methods have been developed to detect diquat in water at concentrations well below the HBV. For example, high-performance liquid chromatography with ultraviolet absorbance detection after solid sorbent cartridge extraction has a detection limit of 1 µg/L (USEPA, 1997; Ministry of Health, Labour and Welfare, Japan, 2013), and liquid chromatography–mass spectrometry analysis after solid-phase extraction can be applied with a practical quantification limit of 1 µg/L (Ministry of Health, Labour and Welfare, Japan, 2013). Recently, a liquid chromatography with tandem mass spectrometry method has been developed that provides a method reporting limit of 0.1 µg/L for diquat in water (Hao et al., 2013).

7. TREATMENT TECHNOLOGIES

Conventional treatment, including coagulation and filtration, is not effective for reducing the concentration of diquat in water. Activated carbon may be effective for the removal of diquat (USEPA, undated; Parkash, 1974; Speth & Miltner, 1998). The adsorption efficacy of diquat is highly dependent upon the pH of the water, as diquat has a 2+ charge below pH 10 (Speth & Miltner, 1998). Therefore, the removal mechanism for diquat in activated carbon systems is likely due to ion exchange phenomena rather than to typical hydrophobic sorption.

8. CONCLUSION

It is not considered necessary to establish a guideline value for diquat, as it occurs in drinking-water sources or drinking-water at concentrations well below those of health concern. Where monitoring results show the presence of diquat in drinking-water on a regular basis, an HBV of 0.03 mg/L can be applied. In an emergency or spill situation, an acute HBV of 20 mg/L may provide useful guidance.

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