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Probabilistic risk assessment of veterinary medicines applied to four major aquaculture species produced in Asia

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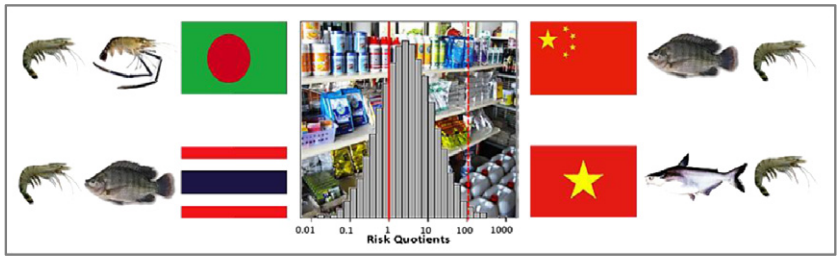
HIGHLIGHTS

- A risk assessment was performed for eight aquaculture production scenarios in Asia.
- About 25% of the applied mass of veterinary medicines is released to the environment.
- Cultured species density and water exchange rates correlate with environmental release.
- Overall, aquaculture parasiticides show higher ecological risks than antimicrobials.
- *Pangasius* production in Vietnam represents the highest ecological risk.

GRAPHICAL ABSTRACT



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ABSTRACT

Aquaculture production constitutes one of the main sources of pollution with veterinary medicines into the environment. About 90% of the global aquaculture production is produced in Asia and the potential environmental risks associated with the use of veterinary medicines in Asian aquaculture have not yet been properly evaluated. In this study we performed a probabilistic risk assessment for eight different aquaculture production scenarios in Asia by combining up-to-date information on the use of veterinary medicines and aquaculture production characteristics. The ERA-AQUA model was used to perform mass balances of veterinary medicinal treatments applied to aquaculture ponds and to characterize risks for primary producers, invertebrates, and fish potentially exposed to chemical residues through aquaculture effluents. The mass balance calculations showed that, on average, about 25% of the applied drug mass to aquaculture ponds is released into the environment, although this percentage varies with the chemical's properties, the mode of application, the cultured species density, and the water exchange rates in the aquaculture pond scenario. In general, the highest potential environmental risks were calculated for parasitic treatments, followed by disinfection and antibiotic treatments. *Pangasius* catfish production in Vietnam, followed by shrimp production in China, constitute possible hot-spots for environmental pollution due to the intensity of the aquaculture production and considerable discharge of toxic chemical residues into surrounding aquatic ecosystems. A risk-based ranking of compounds is provided for each of the evaluated scenarios, which offers crucial information for conducting further chemical and biological field and laboratory monitoring research. In addition, we discuss general knowledge gaps and research priorities for performing refined risk assessments of aquaculture medicines in the near future.

1. Introduction

During the last decades, the production of aquatic food in the Asian continent has experienced an unprecedented increase and nowadays accounts for about 90% of the global aquaculture production (FAO,

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2012). The great majority of the Asian aquaculture is produced in land-based freshwater or brackish water ponds, which rely on periodic effluent discharges into surrounding water bodies (Bostock et al., 2010). In order to promote optimal health conditions, and to treat and prevent possible disease outbreaks, Asian aquaculture farmers have reported the use of a wide range of veterinary medicines such as antimicrobials, fungicides, anthelmintics and other parasiticides (Bondad-Reantaso et al., 2012; Rico et al., 2012a, 2013a). Residual concentrations of aquaculture medicines used in inland aquaculture farms have been measured in water and sediments of down-stream rivers and estuaries (Le and Munekage, 2004; Zou et al., 2011), and constitute an important source of environmental pollution (Boxall et al., 2004).

Aquaculture pharmaceuticals and other potentially toxic chemicals may result in harmful effects on the biodiversity and functioning of aquatic ecosystems surrounding aquaculture farms, and may compromise the environmental sustainability of the aquaculture sector. To assess the potential ecological effects of veterinary medicines used in aquaculture, environmental risk assessment schemes have been established and implemented in the registration and evaluation procedures of veterinary medicinal products in many developed countries (VICH, 2000, 2004). Such environmental risk assessment procedures, however, have not yet been adopted in the main aquaculture producing countries of (sub-) tropical Asia, and the number of independent studies investigating the environmental occurrence and ecological risks of aquaculture medicines in the Asian continent is still very limited in comparison to other, temperate, regions. Although concerns have been recently raised about the potential ecological implications of the intensive use of chemicals in Asian aquaculture (Gräslund and Bengtsson, 2001), consistent data on their environmental fate following use in aquaculture farms and potential ecological risks have never been generated (Thuy et al., 2011; Rico et al., 2012a). Given the large number of chemical treatments used in Asian aquaculture and the wide range of species and aquaculture production scenarios, prioritization approaches need to be used to guide scientific research and economic investments, especially in situations of limited prospective environmental risk regulation and monitoring resources.

In the current study we assessed the potential ecological risks posed by the use of veterinary medicines in eight aquaculture grow-out pond scenarios in Asia. The eight scenarios included in the present study represent shrimp production in Bangladesh, China, Thailand, and Vietnam; prawn production in Bangladesh; tilapia production in Thailand and China; and *Pangasius* catfish production in Vietnam. These aquaculture farm groups were selected because of their relative increase in production volume over the last decades and the availability of up-to-date data on the use of veterinary medicines and farming practices (Rico et al., 2013a). A probabilistic risk assessment was performed by combining information on the use of veterinary medicines in each of the studied aquaculture scenarios, chemical properties of the evaluated substances, and characteristics of the modelled aquaculture pond scenarios. Risk calculations were performed by using the ERA-AQUA v2.0 model, a mass balance model designed to calculate environmental exposure and risks of veterinary medicines applied in pond aquaculture scenarios (Rico et al., 2012b, 2013b). Chemical exposure profiles in the aquaculture farm effluents were used to calculate acute and chronic risks for primary producers, invertebrates, and fish in adjacent aquatic ecosystems (Fig. 1). The main objectives of the present study were to prioritize compounds, scenarios, and biological taxa that should be targeted in specific ecotoxicological and field monitoring studies, as well as to identify data gaps and research needs that must be addressed in the future in order to perform refined risk assessments for veterinary medicines in Asian aquaculture.

2. Material and methods

2.1. Chemical use data

Forty-seven veterinary medicinal treatments were evaluated in the current study including antibiotics, disinfectants and parasiticides. This list of chemical treatments is based on a survey on chemical use practices performed, during 2011 and 2012, to 252 aquaculture grow-out farmers and 56 farm supply shops corresponding to the countries and aquaculture farm groups included in the current study (for details see Rico et al., 2013a). The list includes chemicals applied directly to water for disinfection of the culture facilities prior to stocking, and chemicals applied either directly to water or mixed with feed for disease treatment or prevention during the culture cycle. The list of chemical treatments evaluated in the present study, mode and frequency of use, recommended dosage, and duration of the treatment period is shown in Table S1. When the recommended dosage and the duration of the treatment were reported as a numeric interval, the highest value was conservatively chosen for the risk assessment calculations.

2.2. Chemical properties

2.2.1. Physico-chemical properties

Information on the physico-chemical properties of the veterinary medicinal ingredients was retrieved from online databases (e.g. http://sitem.herts.ac.uk/aeru/vsdb/index.htm; http://www.chemspider.com), and the literature. Information was collected for the following parameters: molecular mass, octanol–water partition coefficient, sorption coefficient to organic carbon, solubility and reference temperature at which it was determined, enthalpy of dissolution, saturated vapour pressure and temperature at which it was determined, enthalpy of vaporization, half-life degradation of the substance in water and sediment and temperatures at which they were determined, and molar Arrhenius activation energy. When data were not available for the enthalpy of dissolution, the enthalpy of vaporization, or the Arrhenius activation energy, the default values included in the ERA-AQUA model by Rico et al. (2012b) were used. When the required data were not available for the rest of the chemical properties listed above, they were calculated according to the Quantitative Structure–Activity Relationship (QSAR) models included in the EPI Suite v4.1 software (US EPA, 2012). The resulting dataset of physico-chemical properties for the evaluated compounds is presented in Table S2.

2.2.2. Pharmacokinetics data

Data on biological half-lives (BioT1/2) in fish and crustaceans for the evaluated compounds were retrieved from the PhishPharm database (Reimschuessel et al., 2005). We only selected studies in which the BioT1/2 values were calculated based on measured concentrations in muscle, and muscle and skin samples, and in which the compound was administered via bath immersion, oral gavage or mixed with feed. This data selection resulted in 218 BioT1/2 data entries. In order to minimize the influence of the experimental set-up in which they were calculated, the BioT1/2 values were normalized to an organism weight of 0.1 kg and a temperature of 20 °C, according to the equation described in Arnot et al. (2009). The normalized BioT1/2 values were classified into four categories according to the aquaculture species group (fish or crustaceans) and the drug administration method (oral administration or administration via water exposure). Subsequently, the available BioT1/2 values within each of these four categories were further classified into chemical classes according to the nature of the active ingredient. The classification yielded 13 different compound classes for antibiotics and anthelmintics applied mixed with feed or in oral gavage (aminoglycosides, aminopenicillins, amphenicols, avermectins, cephalosporins, diaminopyrimidines, heterocyclic acetic acid derivatives, polypeptides, pyrazinaisoquinolines, quinolones, rifampicins,