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Short communication

Ecotoxicity and carbon footprint of commonly used antibiotics: Moving towards environmentally sustainable use

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ABSTRACT

Introduction: The environmental impact of antibiotics is described as high, although it has never been precisely assessed. We evaluated the environmental impact of some antibiotics.
Methods: Environmental impact was measured by (*i*) carbon footprint (CF) through Life Cycle Assessment and (*ii*) ecotoxicity, assessed by the Risk Quotients for the risk of antimicrobial resistance development (RQ-R), calculated from median environmental concentrations and theoretical Predicted No-Effect Concentrations (PNECs).
Results: Production of antibiotics in Europe reduces CF compared to production in Asia. Intravenous (IV) levofloxacin has a higher CF than per os levofloxacin. IV push has a lower CF than IV drip administration. Ceftriaxone and azithromycin have respectively a lower CF than cefotaxime and clarithromycin. Although co-trimoxazole CF is higher than that of fluoroquinolones, its RQ-R is lower.
Conclusion: Although discrepancies between CF and eco-toxicity limit recommendations, these two parameters may guide decisions to reduce environmental footprint in a One-Health approach.

1. Introduction

Climate change is associated with major public health consequences, with infectious diseases at its core [1]. The World Health Organization (WHO) identifies climate change and antimicrobial resistance (AMR) as the two main threats to human health [2,3]. The healthcare sector emits greenhouse gases, estimated in France to account for approximately 8% of national emissions [4]. Pharmaceuticals and medical devices represent the largest contributors and account for half of total emissions [4]. Beyond the carbon footprint (CF) of production, pharmaceuticals excreted by patients or during manufacturing can enter wastewater, altering ecosystems and favoring the emergence and persistence of AMR in the environment [5]. Infectious disease specialists advocate for an ecological transition in healthcare, calling for integrating environmental criteria (CF, ecotoxicity, and risk of AMR development in the environment) into clinical practices [6]. However, the environmental impact of prescribed antibiotics is largely unknown to prescribers. Here, we assessed the environmental footprint of eight widely used antibiotics.

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2. Methods

Environmental criteria were evaluated for cefotaxime, ceftriaxone, levofloxacin, ciprofloxacin, ofloxacin, co-trimoxazole (combination of sulfamethoxazole and trimethoprim), azithromycin, and clarithromycin (Table S1). The CF was estimated using a cradle-to-pharmacy-gate Life Cycle Assessment (LCA) method [7–9], accounting for greenhouse gas emissions with the production of Active Pharmaceutical Ingredients (API), excipients, packaging, emissions from manufacturing plants, and import to France. The cradle-to-pharmacy-gate boundaries were selected because the use phase of solid oral antibiotics has a negligible climate impact (only requiring a glass of water and no medical devices) while the end-of-life stage (disposal of the paper leaflet, cardboard, and primary packaging) contributed similarly across all studied solid oral antibiotics. In contrast, when comparing intravenous (IV) formulations, the use phase was included in the system boundaries because administration of injectable drugs is associated with greater environmental impact. The focus was on antibiotics commonly prescribed for urinary and respiratory tract infections. Therapeutically comparable treatments were selected to make comparisons based on environmental criteria. These included comparisons between co-trimoxazole and fluoroquinolones for urinary tract infections, between two third-generation cephalosporins (cefotaxime and ceftriaxone), and between two macrolides (azithromycin and clarithromycin). We compared the CF of production in Asia to that of production in Europe using a Wilcoxon rank-sum test. The use phase was assessed for IV antibiotics which required medical devices (Table S2). For IV administration, a slow IV infusion over 30 to 60 min with dilution in 100 mL of saline was compared to direct IV administration with dilution in 10 mL of saline (Table S2). API synthesis routes were obtained from the environmental statements of producers, patents, and scientific literature [8]. Packaging components were precisely weighed. The results were expressed in gCO_2eq/DDD (Defined Daily Dose). DDD is the reference daily dose, representing the usual adult (70 kg) dosage for the main indication of the active ingredient.

Environmental toxicity was assessed by calculating Risk Quotients (RQ). RQ are the ratios of measured environmental concentrations (MECs) of antibiotics in treated wastewater in France and Predicted No-Effect Concentrations for the environment (PNEC-ENV) or for resistance (PNEC-R) [10,11]. MECs were available for all antibiotics except for ceftriaxone and levofloxacin. RQ for ecotoxicity was defined as MECs/PNEC-ENV, and RQ for the risk of AMR development as MECs/PNEC-R [10,11]. High, medium, and low risks were defined by RQ values of >1, 0.1 to 1, and < 0.1, respectively (Table S3).

3. Results

3.1. Breakdown of CF

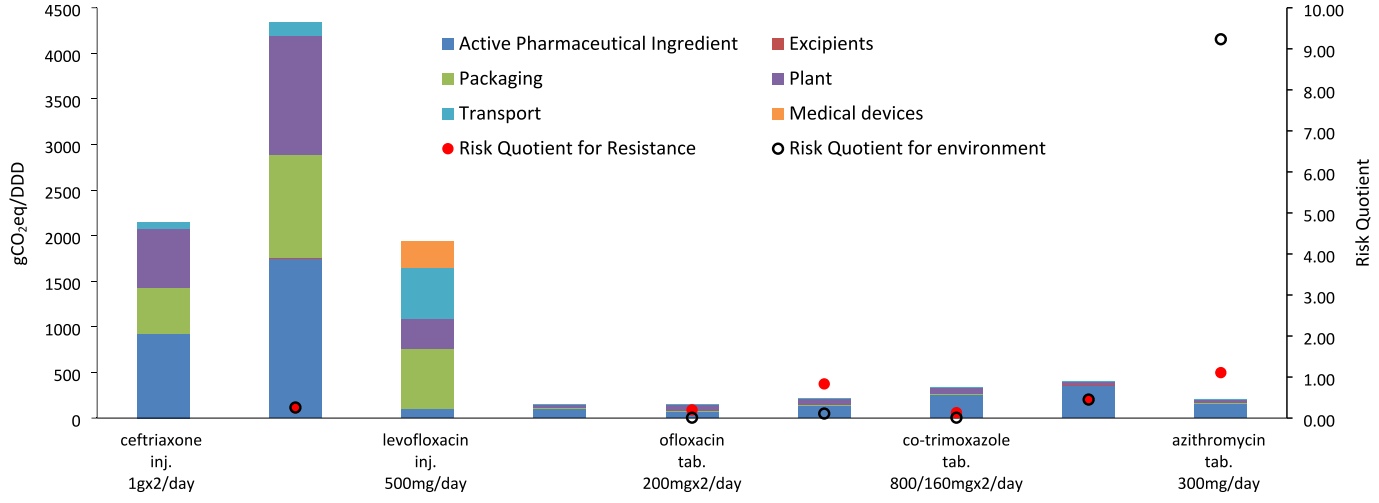
CF of antibiotics is primarily driven by API production (40–89%), followed by manufacturing emissions (19–43%), and packaging (23–40%) (Fig. 1). Transport and excipients account for <1% of the CF (Figs. 1 and 2A), except for IV levofloxacin, where transport accounts for 34% due to the heavy ready-to-use infusion bags (Fig. 2B).

3.2. Comparison by place of manufacture

As exemplified by cefotaxime production (Fig. 2A), CF of European manufacture is lower than that of Asian manufacture ($p = 0.007$), with a median reduction of 27.7% [interquartile range 22.7–28.3] driven by lower emission factors for energy and solvent production (Fig. S1).

3.3. Comparison by route of administration

- Oral *versus* IV administration: despite equal clinical efficacy, IV administration of levofloxacin exhibits a 13-fold increase in CF compared to oral administration (Fig. 2B) due to more packaging, transport, and manufacturing emissions.
- Direct IV *versus* slow IV administration: for third-generation cephalosporins, direct IV administration requires fewer medical devices than slow IV administration and therefore has one quarter of the CF, while maintaining comparable clinical efficacy (Fig. 2C and Table S4) [12]. Hence, direct and slow IV administration of ceftriaxone provide similar efficacy for uncomplicated urinary tract infections, excluding critical care cases. However, direct IV administration has a CF of 134 gCO_2eq compared with 666 gCO_2eq



Inj.: injectable, tab: tablet

Fig. 1. Environmental footprint of various antibiotic molecules manufactured in India (carbon footprint and ecotoxicity). Environmental footprint was measured by carbon footprint (CF), according to the GHG protocol, assessed by Life Cycle Assessment and expressed in gCO_2eq/Defined Daily Dose (DDD); and eco-toxicity, assessed by the Risk quotients (RQ) for aquatic environments and for resistance, which are based respectively on the ratio of the median environmental concentrations measured in treated wastewater in France (median-MEC) to the Predicted No-Effect Concentrations for environment (PNEC-ENV) and for antimicrobial resistance (PNEC-R) [3]. RQs for ceftriaxone and levofloxacin could not be determined due to the absence of median-MECs. As co-trimoxazole combines two antibiotics, we display the highest RQs of the two compounds (RQ for environment of sulfamethoxazole, RQ for resistance of trimethoprim). High, medium, and low risks were defined by RQ values >1, 0.1 to 1, and < 0.1, respectively.

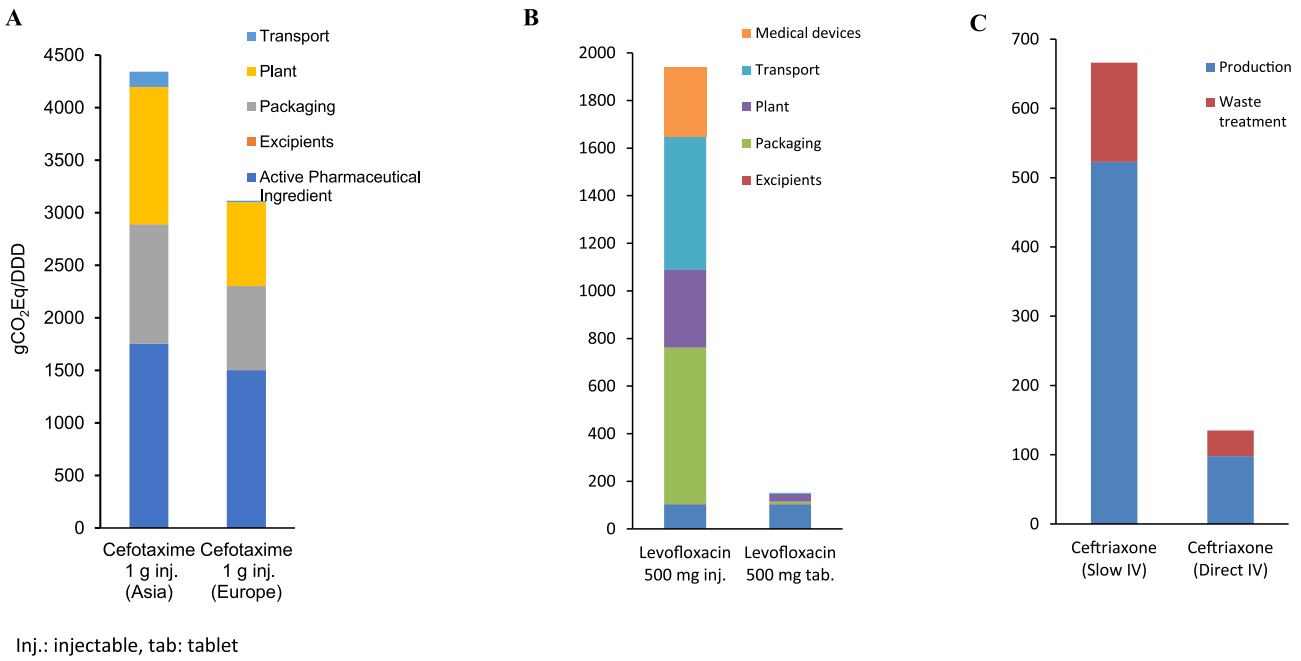


Fig. 2. Comparison of the carbon footprint of antibiotics according to location of production and routes of administration.
Comparison of carbon footprint (expressed in gCO_2eq/Defined Daily Dose - DDD) of 1 g of cefotaxime produced in Asia or Europe (A), of 500 mg of levofloxacin as injectable solution or tablet (B), and of ceftriaxone 1 g injected through slow intravenous injection in 100 ml of saline (slow IV) or direct intravenous injection in 10 ml of saline or water (direct IV) (C).

for slow IV infusion. In addition, the direct IV route reduces nursing workload and improves patient comfort (Tables S2 and S4). Similar findings were observed for cefotaxime (Tables S2 and S4).

3.4. Impact of DDD on CF

The CF of an antibiotic not only depends on the environmental impact of the API production, but also on its DDD. Thus, while ciprofloxacin's API has a lower CF than ofloxacin, its CF per day of treatment (expressed in gCO_2eq/DDD) is higher due to a higher DDD (Tables S5 and S6).

3.5. Comparison of antibiotics within the same therapeutic class

Antibiotics from the same family, with similar clinical use and dosage, can differ in CF. For instance, ceftriaxone has a lower CF than cefotaxime, with a similar efficacy (Fig. 1) [12]. The RQs for ceftriaxone are absent because MECs were not available. However, the ecotoxicity of these two cephalosporins is likely low, given their rapid degradability in the environment [10].

3.6. Comparison of antibiotics from different therapeutic classes

In urinary tract infection treatment, one day with ofloxacin or ciprofloxacin has a lower CF than with co-trimoxazole, but higher ecotoxicity. In pulmonary infection treatment, azithromycin has a lower CF than clarithromycin but higher ecotoxicity due to higher MECs and lower PNEC-ENV (Fig. 1, Table S3). Hence, knowledge of the environmental impact of clinically equivalent antibiotics could help guide prescriptions.

4. Discussion

This study showed that (*i*) CF of antibiotics is mainly due to API production, (*ii*) CF is lower for European manufacture than for Asian manufacture, (*iii*) DDD is a higher contributor to environmental impact than manufacture of API; (*iv*) oral levofloxacin has a lower CF than the IV route, (*v*) direct IV has a lower CF than slow IV, (*vi*) CF and ecotoxicity of a given antibiotic can diverge, and (*vii*) CF and ecotoxicity can vary within the same antibiotic family.

This first evaluation of CF and ecotoxicity of antibiotics could help reduce the environmental impact of medicines while maintaining quality of care. LCA is a validated, robust, and reproducible methodology to measure CF [7]. The contribution of antibiotic residues to the emergence of AMR in the environment is often overlooked, despite being a clear illustration of the One Health concept [1,2]. Thus, this study lays the foundation for an antibiotic-specific eco-score, primarily intended for prescribers and purchasing pharmacists, but also to raise awareness among patients. This eco-score accounts for the risk of AMR in the environment and could complement the Swedish PBT (Persistence, Bioaccumulation, Toxicity) index, which is based on resistance to degradation, accumulation in and toxicity for aquatic organisms [13,14].

This study has several limitations. First, as most suppliers declined to provide information, most data were retrieved from patents and environmental declarations from manufacturers. Second, storage and distribution of the antibiotics, the use phase of oral drugs and the end-of-life of medicines (packaging waste treatment, API excretion) were not considered, as they are similar for all antibiotics and emit few greenhouse gases. Third, corporate emissions from head offices and research and development were excluded, since accounting for 3–14% of antibiotic emissions in this study [15]. Furthermore, the single-impact LCA only considers carbon emission, excluding other environmental impacts. To evaluate ecotoxicity, we used antibiotic concentrations in French wastewater. Although the data may not be representative of all settings, it should be comparable across high-income countries [10]. We did not assess the risk of AMR in the sewage sludge produced by wastewater treatment plants, in which antibiotics can accumulate [5]. In accordance with the precautionary principle, we used the lowest reliable PNEC-R, calculated from the minimum inhibitory concentrations determined in vitro in monoculture in rich media [11]. However, these theoretical PNEC-R, often much lower than PNEC-R measured with bacterial community in complex matrices, may overestimate the risk of AMR development in the environment [16].

Our results support the relocation of antimicrobial production to Europe, which could also strengthen supply chain resilience and reduce the risk of shortages. Based on our findings, the oral route should be favored whenever clinically appropriate, for its environmental benefits, but also to minimize the risk of catheter-related infections and to decrease nursing workload. Comparing different antibiotics remains challenging due to inconsistencies between CF and ecotoxicity and lack of in vitro data, which underscores the urgent need for MECs and experimentally determined PNECs. In addition, there is no consensus on how to evaluate the impact of antibiotics on the patient's microbiota and the associated risk of promoting AMR, which limits the integration of these factors into clinical decision-making. These aspects will be key criteria when selecting an antibiotic regimen for a given patient, alongside the strain resistance profile, the ability of the antibiotic to select resistance in vivo, and its diffusion to the infection site.

When more comprehensive and reliable data are available, developing guidelines that account for these multiple criteria will require multidisciplinary input and the creation of a standardized eco-score for prescribers. This antibiotic-specific eco-score could include several criteria, including CF, RQ for ecotoxicity (MECs/PNEC-ENV), RQ for the risk of AMR development (MECs/PNEC-R), antibacterial spectrum, and impact on the gut microbiota. By integrating these parameters into a composite metric, the eco-score would support the selection of antibiotics that achieve the most favorable balance. Because no antibiotic is likely to perform optimally across all criteria, the eco-score would provide a framework for weighing trade-offs among environmental persistence, ecotoxicity, AMR selection, spectrum of activity, and microbiota disruption. The preferred antibiotic would not necessarily be the one with the lowest value for every individual criterion, but rather the one with the most favorable overall environmental profile among therapeutically equivalent alternatives. Pending the development of an antibiotic-specific eco-score, this study demonstrated that antibiotic administration protocols can be optimized by prioritizing the oral route—when bioavailability is equivalent—and the direct intravenous route over the slow intravenous route. Based on these CF results, continuous antibiotic infusions may reduce CF compared with intermittent infusions.

5. Conclusion

This preliminary study lays the groundwork for developing an eco-score specific to antibiotics by assessing environmental impact (CF, ecotoxicity, and risk of AMR development in the environment) of eight widely-used antibiotics. Further research is needed to generate reliable, reproducible, multilevel data, a prerequisite for incorporating such criteria into future guidelines and clinical practice. Accounting for the environmental footprint of antibiotics would inform decisions aimed at reducing emissions while preserving the same standard of patient care.

Authors contribution

A.C., V.P., E.P., F.B., C.B., and M.R.I. designed the study. S.T. and N. N. carried out the carbon footprint study using life cycle assessments. M. R.I., V.P., A.-L.B., and D.H. analyzed the data. M.R.I wrote the original draft. M.R.I., A.-L.B., and D.H. reviewed and edited the manuscript. A.-L. B. created the graphic summary. All the authors approved the final version.

Ethical statement

The authors certify that all procedures were performed in accordance with laws and ethical guidelines. Approval from an ethics committee was not required.

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Transparency declarations

None to declare.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.idnow.2026.105354.

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