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Special article

[Translated article] Pharmaceuticals in the environment: A hospital pharmacy perspective

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ABSTRACT

Drugs do not disappear once they have been excreted. In fact, 992 active principles have already been measured in the different environmental matrices. A recent study led by scientists from the University of York has studied the presence of drugs in the rivers of more than 100 different countries, showing that environmental contamination by pharmaceuticals is a global issue and that, concentrations found are frequently harmful to the environment.

In this work, we have tried to briefly expose the problem of environmental contamination with medicines, but above all, we have tried to address the possible solutions, with a perspective from the field of hospital pharmacy. This is a very complex matter (a wicked problem), since it involves multiple stakeholders with different visions and interests regarding medicines. In order to find solutions, we will probably need to act at all steps of the drug's life cycle. Until now, health professionals have been part of the problem. It is time for us to be part of the solution.
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El impacto ambiental de los medicamentos: una mirada desde la Farmacia Hospitalaria

Palabras clave:
Contaminantes de interés emergente
Fármacos y medio ambiente
Objetivos de desarrollo sostenible
Contaminación ambiental

RESUMEN

Los fármacos no desaparecen una vez han sido excretados. De hecho, ya se han medido 992 principios activos en las diferentes matrices ambientales. Un reciente estudio liderado por científicos de la Universidad de York ha estudiado la presencia de fármacos en los ríos de más de 100 países diferentes, demostrando que la contaminación ambiental por fármacos es un asunto global y que, además, las concentraciones halladas resultan ser con mucha frecuencia dañinas para el medio ambiente.

En este trabajo se ha intentado exponer brevemente el problema de la contaminación ambiental con medicamentos, especialmente abordando las posibles soluciones, con una perspectiva desde el ámbito de la farmacia hospitalaria. Se trata de un asunto muy complejo, ya que implica a múltiples agentes con visiones e intereses muy diferentes acerca de los medicamentos. Para poder buscar soluciones, probablemente se necesitará actuar en todos los pasos del ciclo de vida del medicamento. Hasta el momento los profesionales sanitarios hemos sido parte del problema. Es hora que formemos parte de la solución.

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Introduction

In the late 1990s, a forest ranger in the Rajasthan region of northern India was stunned and bewildered to find that half of the vultures in Keoladeo National Park had died. He decided to publish the results of his research in a local journal.[1] When he realised that a few years later not a single one remained, he decided to contact colleagues across the country to see what was happening. The results of the research were extremely alarming. The population of the Bengali white-backed vulture (*Gyps bengalensis*), then the most abundant bird of prey on earth, had suffered a catastrophic collapse and was on the verge of extinction.[2] In fact, it was the most rapid population decline of any bird ever recorded in history. Within a few decades, tens of millions of vultures had died out. The cause of such a disaster was an absolute mystery to the scientific community. Lack of food did not seem to be a factor, so given the geographical distribution, an infectious cause was initially thought to be the cause: a virus to which the vultures had never been exposed? A virus totally unknown to science? Finally, a research team led by Lyndsay Oaks, a young American veterinary microbiologist, found the cause. The results, which came as a real surprise, were published in the journal *Nature*. The cause turned out to be diclofenac, a non-steroidal anti-inflammatory drug for veterinary use. This drug turned out to be extremely nephrotoxic to these necrophagous birds, causing visceral gout and death.[3]

Although almost 20 years have passed since then, a survey conducted at the Faculty of Pharmacy in Vitoria-Gasteiz (Spain) showed that the vast majority of students had not heard of this event.[4] Up to now, the environmental impact of medicines has mainly been addressed by environmental specialists (biologists, chemists, etc). However, we are now at a turning point when environmental issues are becoming increasingly relevant at the societal level. It is also time to look at the problem from the perspective of hospital pharmacy and be part of the solution.

Magnitude of the problem

Presence of pharmaceuticals in the environment

In both human and veterinary healthcare, the consumption of pharmaceuticals is increasing.[5] Once excreted, pharmaceuticals reach wastewater treatment plants (WWTPs) in the best case scenario, but these plants are primarily designed to remove organic matter rather than micropollutants such as pharmaceuticals. It is therefore not surprising to find pharmaceuticals in rivers, lakes (surface water), groundwater, coastal waters, and even in our drinking water. In addition to such water bodies, pharmaceuticals are also found in solid media such as soil and, above all, sewage sludge.

The German Federal Environment Agency (UBA)[6] collects information on the presence of pharmaceuticals, metabolites, and transformation products in different environmental matrices. These substances are produced in the environment through biological processes, such as the metabolism of various organisms including bacteria, as well as through physico-chemical processes such as exposure to UV light. The database is regularly updated and is available free of charge. The latest version, which includes data available until 2021, describes the presence of 992 different drugs in the environment. Almost all drugs from all therapeutic groups have been measured, but the most extensively studied are antimicrobials, anti-inflammatory drugs, psychotropic drugs, and cardiovascular drugs. Fig. 1 shows how drugs enter the environment.

A recent study, led by the University of York (UK), which monitored more than 250 rivers in over 100 countries worldwide, showed that drug pollution is a global problem. The most polluted areas are those where income levels are sufficient to support increased drug consumption, but not sufficiently high to build sewage networks and WWTPs.[8] In Spain, samples have been collected from the Manzanares river, which showed relatively high levels of pollution. Other studies have shown that pharmaceuticals are present in practically all of the Spanish nature reserves that have been studied.[9]

Presence in biota. Bioaccumulation

Similar to other pollutants, certain drugs can accumulate in living organisms, sometimes reaching concentrations higher than those found in the surrounding environment.

A study conducted in Germany, the Czech Republic, and the UK analysed the presence of more than 90 pharmaceuticals in the blood plasma of various species of wild fish caught in rivers. Some Czech fish were found to have plasma concentrations of risperidone and flupentixol higher than human therapeutic plasma concentrations.[10]

Another study investigated the presence and concentrations of drugs in 5 rivers in the Melbourne area (Australia). The study also analysed the degree of drug accumulation in various aquatic organisms. The amount of insects ingested by platypuses and brown trout (which are insectivorous) was then used to estimate the drug dose that would be ingested. It was found that for some drugs, such as antidepressants, the dose consumed was up to half the recommended human dose.[11] For more detailed information, see the review published by Miller et al.[12]

Bioaccumulation can also occur in the terrestrial environment, as has been shown for ivermectin in dung beetles in Doñana National Park (Spain).[13]

When lower drug concentrations are observed at the outlets of WWTPs (effluent) than at the inlets (influent), it could be assumed that this due to drugs being removed, mainly through metabolisation by bacteria during secondary treatment. This is often the case, but sometimes, the unchanged drug is adsorbed to the suspended matter and becomes part of the sludge. The sludge can then be used as a fertiliser in agriculture, potentially leading to the transfer of drugs to the vegetables we eat. Similarly, if treated wastewater is used for irrigating crop fields, certain pharmaceuticals could cross into plant tissue. The latter appears to be the reason why 75% of participants (including pregnant women) in an Israeli study, none of whom were taking carbamazepine, had measurable levels of the drug in their urine.[14] The people who ate the most vegetables had the highest levels of the antiepileptic drug. Although the concentrations found are very low (in the order of a few ng/L), these are alarming results, given that carbamazepine is a drug classified as hazardous by the US National Institute for Occupational Safety and Health (NIOSH). Climate change is expected to increase the consumption of treated water for crop irrigation, especially in more arid countries, and this may lead to its increased presence in vegetables.[15]

Ecotoxicological effects

An analysis of the ecotoxicological risk of concentrations reported by a global monitoring study of pharmaceuticals showed that approximately 43.5% of the 1052 sampling locations monitored in 104 countries had drug concentrations of concern.[16]

A fundamental aspect of understanding the ecotoxicological effects of pharmaceuticals once they reach the environment is to adopt an

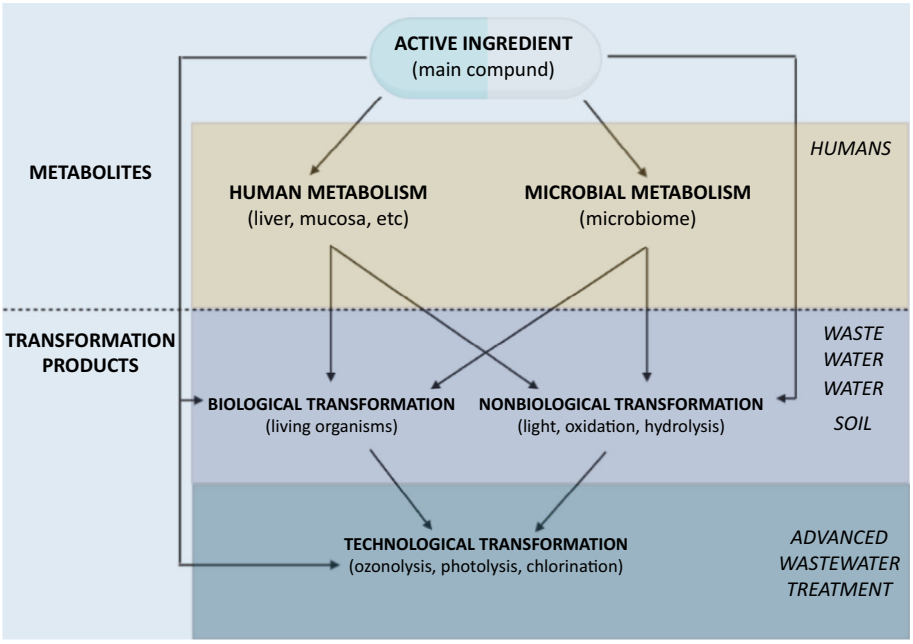

Fig. 1. Metabolites and transformation products of pharmaceuticals. (Source: Kümmerer K.[7])

evolutionary perspective. It should be borne in mind that although human drugs are designed to be active in our species, we share numerous pharmacological targets (enzymes, receptors, etc) with a vast number of living organisms.[17] Take statins, for example, which are among the most widely prescribed drugs for human use in Western European countries. They are used as lipid-lowering drugs because they inhibit 3-hydroxy-3-methyl-glutaryl-CoA reductase, which is the key enzyme in hepatic cholesterol synthesis. However, Akira Endo discovered statins while searching for antimicrobial agents by studying soil micro-organisms, namely fungi of the genus *Penicillium*.[18] Could statins therefore be considered as antimicrobials converted into lipid-lowering agents? Even more interestingly, it turns out that the enzyme it inhibits is phylogenetically highly conserved. In other words, the same enzyme (or very similar versions) is present in all animals. Statins can therefore potentially inhibit cholesterol synthesis in all animals. In this sense, ecologically relevant concentrations of simvastatin (i.e. concentrations in the range of those commonly found in the environment) can inhibit the shedding of the exoskeleton of certain crustaceans.[19]

The combination of different pharmaceutical substances and targets is enormous. For more detailed information, see: https://ecodrug.org/. It is currently estimated that information on the ecotoxicological risk of 88% of marketed drugs is unknown.[20]

An exhaustive review of all the ecotoxicological effects studied is beyond the scope of this paper. However, we have to be mindful of the close interrelationship between animals, humans, and ecosystems (the One Health philosophy), and understand that by disturbing the balance between them, we may end up damaging our own health. For example, the virtual disappearance of the vulture population in the Indian subcontinent has had the collateral effect of increasing the stray dog and rat populations, and thus the number of cases of rabies and leptospirosis.[21]

Moreover, antimicrobial resistance is a global public health crisis that threatens the ability to successfully treat bacterial infections.[22] The 'tragedy of the commons'[23] is a term used in the social sciences—now adapted to the field of antibiotics—to describe a situation in which several individuals use a common good, but end up acting only out of self-interest and destroying it, even when it is in no one's interest to do so. The overuse of antibiotics in the medical, veterinary, and agricultural sectors may be the root cause of the development of antimicrobial resistance worldwide. The problem has been exacerbated by the rash over-the-counter sale of antibiotics in some countries, inadequate sanitation, and the release of unmetabolised antibiotics or their residues into the environment via faeces/manure and industrial effluent.[24] Furthermore, in 2018, the first systematic screening of drugs against a reference panel of human gut bacteria was published.[25] A total of 27% of non-antibiotic drugs inhibited the growth of at least one species. Researchers and pharmaceutical companies should be able to quantify the contribution of non-antibiotic drugs (antidepressants, statins, antipsychotics, etc) to antibiotic resistance. It is obvious that the presence of drugs in the environment is a contributing factor to the emergence of resistance.[26]

Possible solutions

The problem of environmental drug pollution is a complex and multi-factorial issue for which there is no simple solution.[5,27] Beyond becoming aware of the problem, healthcare professionals need to be part of the solution. In this respect, the SEFH's initiative to join the United Nations Global Compact as well as its leadership of the '2023 + SOStenible' initiative are particularly relevant: https://www.sefh.es/sostenible-proyecto.php.

For a more in-depth look at how to tackle the problem from a general perspective, we recommend the excellent review published by Karin Helwig,[28] the GREENER strategy proposed by the European PREMIER project researchers,[29] and the reviews by Caban and Stepanowski[30] and Thornber et al.[31] These publications look in detail at how to reduce the environmental impact of medicines, particularly from a healthcare perspective.

Promoting non-pharmacological measures

The Royal Pharmaceutical Society (UK) has put forward a very good idea: '*The most environmentally friendly medicine is the one that is not required and not prescribed.*'[32] By improving the physical health (exercise, healthy eating, smoking, etc), mental health (mindfulness, psychotherapy, green prescribing, [https://www.england.nhs.uk/personalisedcare/social-prescribing/green-social-prescribing/]), and social health of the population, we will use fewer medicines and, of course, fewer drugs will enter the environment.

Green design

It would be desirable to have effective and safe drugs that are easily degradable once they enter the environment.[33] This is the concept of 'benign by design.' Nevertheless, this is a highly complex task, because drugs are designed to have a certain degree of stability that allows them to be used for therapeutic purposes. For example, the fluorine atom is often used for this purpose. This means that, according to the definition adopted, many drugs could be considered per- and polyfluorinated alkyl substances (PFAS), known for their high persistence in the environment.[34] Some examples are shown in Fig. 2. There is currently a debate on how this issue should be regulated: https://www.efpia.eu/media/636866/pfas-position-_-efpia-and-animalhealtheurope-january-2022.pdf.

Furthermore, the European Commission is currently devoting substantial resources to the development of greener pharmaceuticals and the implementation of more environmentally friendly manufacturing processes. This includes initiatives such as the PREMIER and TRANSPHARM projects. More information is available at: https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/horizon-hlth-2021-ind-07-01.

Buy green. Dispensing medicines associated with telepharmacy

An interesting idea is to integrate environmental criteria into the drug procurement process, prioritising medicines manufactured in more environmentally friendly ways. The carbon footprint of the entire process can be taken into account, including the treatment of waste from laboratories manufacturing drugs in countries such as India or China. For example, see: https://www.sykehusinnkjop.no/nyheter/nyheter-2019/new-environmental-criteria-for-the-procurement-of-pharmaceuticals/. The UK is also working along these lines: https://www.england.nhs.uk/greenernhs/wp-content/uploads/sites/51/2022/03/B1030-applying-net-zero-and-social-value-in-the-procurement-of-NHS-goods-and-services-march-2022.pdf.

On the other hand, we are seeing changes in our daily practice that align with the times in which we live. Telepharmacy, defined as remote pharmacy practice through the use of information and communication technologies, is here to stay. The informed dispensing and delivery of medicines, as a supplement to telepharmacy, aids in decreasing patient travel, thereby reducing the carbon footprint associated with medical dispensing (https://www.sefh.es/mapex/images/Telefarmacia_SEFH.pdf).

Redefining the rational use of medicines

The definition of the rational use of medicines was proposed at a meeting of the World Health Organisation almost 40 years ago. However, the environment is not mentioned in this definition. Recently, a modernisation of this definition has been proposed to incorporate the *One Health* philosophy: 'Patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community, taking into account the interconnectedness of people, animals, plants and their shared environment.'[35]

Ecoprescription

In 2004, a head of the US Environmental Protection Agency, Christian Daughton, proposed a revolutionary idea: that doctors should take environmental criteria into account when prescribing.[36] So far, this idea has not gained much traction, possibly because it was proposed by someone outside the health field. Despite the lack of success, there are some initiatives worthy of mention. On the one hand, there is the Kloka Listan in Sweden, which can be translated as the 'Wise List.' This is a pharmacotherapeutic guideline that stands out because it includes both clinical and environmental criteria (https://klokalistan.se/terapiomrade/aldre-och-lakemedel/angest.html). In addition, the Scottish One Health Breakthrough Partnership initiative is also exploring ways to integrate environmental aspects into clinical decisions. To this end, they have received funding from the Medical Research Council (UK) (https://ohbp.org/).

In essence, incorporating environmental aspects into prescribing could bring about a true Copernican revolution in pharmacotherapy. Although most doctors continue to ignore environmental aspects when prescribing,[37] steps are gradually being taken toward eco-directed sustainable prescribing. Twenty years after Daughton proposed his idea—and presumably without the authors of the guideline having read his article published in the journal *Science of The Total Environment*—the Spanish asthma treatment guideline (GEMA 5.2), among

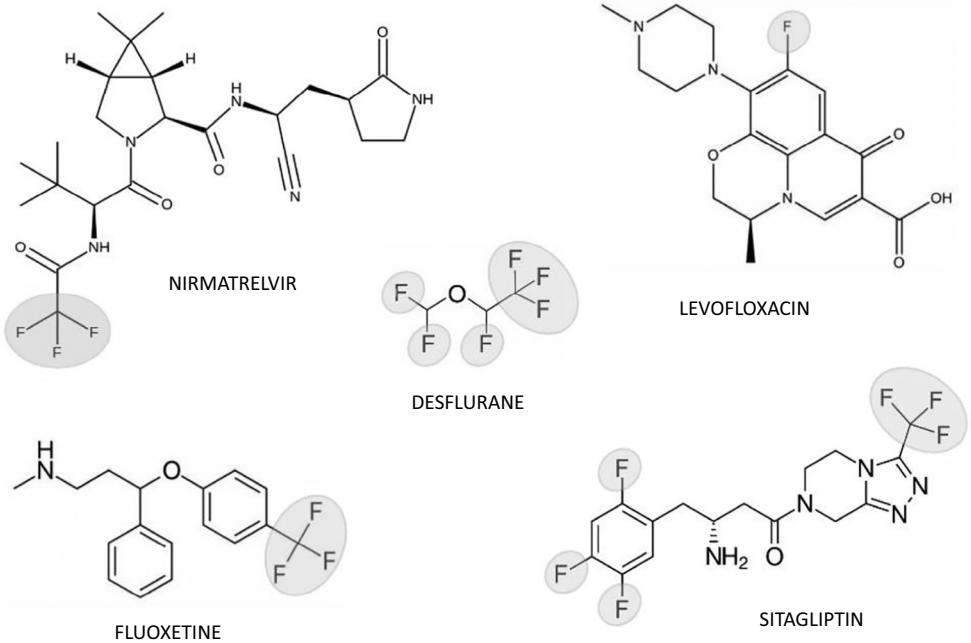

Fig. 2. Drugs that could meet the definition of PFAS: per- and polyfluorinated alkyl substances.

others, states that 'until new propellants with a lower carbon footprint impact are available, the use of dry powder or soft mist inhalers may be preferable in new patients over 6 years old or with inspiratory flow greater than 30 L/min.'

Furthermore, antibiotic optimisation programmes (AOPs) are now regarded as essential tools within the quality of care and patient safety framework of hospitals worldwide. Their implementation and development has been endorsed by national and international scientific societies. In the English-speaking world, they are commonly known as antimicrobial stewardship programmes (AMSPs). Possible strategies to optimise antibiotic therapies and reduce the risk of bacterial resistance include the following aspects: rapid microbiological diagnostics, inflammation marker-guided therapies, shortening the standard duration of antibiotic treatment, tailoring dosing based on pharmacokinetic/pharmacodynamic targets, and avoiding the administration of antibiotics or antibiotic families associated with a higher risk of inducing bacterial resistance.[38] Wang et al. suggested that antibiotic load and the environmental risk for the development of resistance are interrelated phenomena, which must be understood through examination of both hydrological regimes and the environmental fate of antibiotics.[39] ASPs are an essential part of the Spanish National Plan against Antibiotic Resistance (PRAN) (https://www.resistenciaantibioticos.es/es) which, among many other actors, includes the SEFH.

Possible strategies for optimising therapies include the deprescription of inappropriate drugs, which in turn lowers the environmental impact by reducing the unnecessary consumption of medicines and the demand for pharmaceutical production.[40]

Of course, improving adherence to drug treatments will aid in reducing medication wastage. In this respect, hospital pharmacists play a key role (https://gruposdetrabajo.sefh.es/adhefar/index.php/objetivos-del-grupo).

With citizens becoming increasingly concerned about environmental issues, the environmental impact of pharmaceuticals may emerge as a relevant factor in shared decision-making, as evidenced by recent studies conducted in Sweden and the UK.[41,42]

Simplify or reduce

In recent years, the speed at which new synthetic chemicals have appeared on the market has outstripped the capacity to assess their risks. In fact, the diversity and quantity of synthetic chemicals entering our ecosystems has been increasing at a rate that exceeds those of other drivers of global environmental change, such as CO_2 and biodiversity loss. Pharmaceuticals and pesticides are the synthetic chemicals moving most rapidly into ecosystems.[43]

Reducing the supply of available pharmaceuticals, provided there are equally safe and effective alternatives, may be a beneficial approach from both a therapeutic and environmental standpoint.[44]

Regulatory framework. Eco-pharmacovigilance

Clearly, we are at a turning point, especially in Europe, which has likely become the world region where environmental issues have become increasingly prominent. For example, the European Union's 'Strategic Approach to Pharmaceuticals in the Environment' within its well-known Green Deal initiative outlines a relevant framework for action (https://ec.europa.eu/environment/water/water-dangersub/pdf/strategic_approach_pharmaceuticals_env.PDF).

In 2023, the European Commission published a proposed revision of the Water Framework Directive.[45] This revision is novel in that it includes a list of pharmaceuticals as priority substances and establishes concentrations in water (both surface and groundwater) that must not be exceeded (Table 1).

In addition, the Urban Wastewater Treatment Directive, published in October 2022, will require WWTPs to remove at least 80% of a number of pharmaceuticals that are still difficult to remove.[46] The directive specifically names the following drugs: amisulpride, carbamazepine, citalopram, clarithromycin, diclofenac, hydrochlorothiazide, metoprolol, venlafaxine, and candesartan.

Table 1
Pharmaceuticals included in the list of priority substances and their corresponding environmental quality standards.

Environmental quality standards (μg/L)				
	Inland surface waters		Other surface waters	
Priority substance	AA	MAC	AA	MAC
17 α-ethinylestradiol (EE2)	1.7×10^{-5}	–	1.6×10^{-6}	–
17 β-estradiol (E2)	0.00018	–	9×10^{-6}	–
Azithromycin	0.019	0.18	0.0019	0.018
Carbamazepine	2.5	1.6×10^{3}	0.25	160
Clarithromycin	0.13	0.13	0.013	0.013
Diclofenac	0.04	250	0.004	25
Erythromycin	0.5	1	0.05	0.1
Estrone (E1)	3.6×10^{-4}	–	1.8×10^{-5}	–
Ibuprofen	0.22		0.022	
Permethrin	2.7×10^{-4}	0.0025	2.7×10^{-5}	2.5×10^{-4}

AA, annual average; EE2, ethylinyl estradiol; E1, estrone; E2, estradiol; MAC, maximum available concentration.

Since October 2005, the European Medicines Agency (EMA) has required a marketing authorization holder to provide an Environmental Risk Assessment (ERA) report. The result of this report is not taken into account in the risk–benefit assessment, unlike in the case of veterinary medicinal products. Recently, new European pharmaceutical legislation has been published.[47] One the main new features is that failure to submit a full ERA report at the time of application for authorisation may result in a refusal of authorisation. Another novelty is that this regulation includes the creation of an expert working group on environmental impact to advise the Committee for Medicinal Products for Human Use, as is already the case for certain veterinary medicinal products. Also, of interest is the European Commission's proposal on intensifying EU actions to combat antimicrobial resistance in a One Health approach.[48]

On the other hand, many groups are proposing changes to this legislation. In our view, one of the most interesting proposals is that of the Zero Pollution Group, led by Hans Peter Arp, which suggests that the most polluting substances should no longer be sold without a prescription.[49]

There also appears to be a need to establish eco-pharmacovigilance measures. In our view, a historic development has taken place ahead of regulation: Scotland has decided to stop using the anaesthetic gas desflurane. The reason for this is not a lack of safety or efficacy in humans, but for environmental reasons, specifically regarding its carbon footprint! It seems that in the next few years, this measure will be followed at the European level (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52022PC0150). Times are changing. In fact the International Society of Pharmacovigilance (ISOP) has recently created an 'eco-pharmacovigilance' working group to advance in these areas (https://isoponline.org/special-interest-groups/ecopharmacovigilance-group/).

Beyond the active ingredient

One of the most discussed issues, at least in the healthcare field, is the potent greenhouse effect of certain propellant gases used in pressurised inhalers. In Spain, around 52% of inhalers used are pressurised cartridge inhalers, with an average of 15 million units sold per year, resulting in the emission of around 400,000 t of carbon dioxide equivalent per year (https://www.aemps.gob.es/informa/la-aemps-informa-sobre-los-propelentes-utilizados-en-inhaladores-presurizados-y-como-reducir-su-huella-de-carbono/). Curiously, these gases are not included in the ERA report, which refers only to the active pharmaceutical ingredient.[50]

There are many other examples where the environmental impact of the whole medicine is striking. For example, the device that delivers inhaled antipsychotics uses a lithium battery and the entire device is discarded after a single use.[51]

Thus, we will be paying particular attention to the results of the GIMAFH project on the management of inhaler waste from patients with severe asthma, led by the SEFH NEUMO working group. Another interesting project in which the SEFH is also involved is the 'ePIL' electronic leaflet project, which could lead to significant paper savings.[52]

Waste management

The correct disposal of medicines is also a measure of interest. In Spain, SIGRE (https://www.sigre.es/) is the accredited organisation that guarantees the correct environmental management of empty or leftover medicine containers of domestic origin and ensures that all medicine containers marketed through pharmacies in Spain and deposited at SIGRE points receive correct environmental treatment. However, there is currently no accredited system for the collection of veterinary medicines. As the global market for veterinary medicines continues to grow (mainly driven by the growth in the pet medicines market), it is essential that the proper environmental management of these pharmaceuticals can be ensured.

With regard to environmental regulations in hospitals and healthcare centres, the new Royal Decree 1055/2002 of 27 December 2002 on packaging and packaging waste has recently come into force (https://www.boe.es/buscar/doc.php?id=BOE-A-2002-20670). This Royal Decree stipulates that if medicines and their applicators are delivered through health centres, hospitals, or veterinary centres, their waste will be delivered and collected at these centres or at the collection points set up under the Extended Producer Responsibility system. Significant changes in the management of healthcare waste are therefore expected in the coming years.

An initiative of great interest is the 'No unnecessary repackaging' proposal. To avoid repackaging unit doses, automatic systems have been developed to analyse purchases and suggest existing alternatives. For example, in Castilla La Mancha, around 1.2 million repackaged units of medicines have been avoided (https://www.sefh.es/sostenible-proyecto-febrero.php).

Redispensing. Expiration date

Redispensing is a measure that could help to reduce medicine waste. Due to quality and safety concerns, this practice is considered illegal in many areas (e.g. Spain). However, initiatives are already underway to overcome these obstacles by developing humidity and temperature sensors to ensure that dispensed medicines continue to maintain the ideal preservation conditions.[53]

There are other interesting initiatives, such as the PHARMASWAP online platform in the Netherlands, which seeks to prevent the expiration of medicines by linking pharmacies, distribution warehouses, and hospitals (https://www.pharmaswap.com/home-en.html). In Spain, there is the FARMASTOCK initiative in Andalusia or Farmatrueque in Castilla La Mancha (https://www.farmatrueque.com/intranet/acceso_area2.asp).

In addition, a study published by FDA staff on the stability of 122 medicines beyond their expiry dates yielded surprising results. Of the batches analysed, 88% of them extended their expiry dates by more than 1 year, with an average extension of more than 4.5 years[54]!

A clear example of recycling an active ingredient is the capture and reuse of anaesthetic gases such as desflurane and sevoflurane: a device is used to capture the gases emitted by the patient so that they can be reused in future procedures.[55]

Training

It is evident that we cannot allow future generations of healthcare professionals to continue to ignore the fact that drugs do not disappear after the 'E' of excretion in the LADME (liberation, absorption, distribution, metabolism, and excretion,) cycle. To this end, it is essential to incorporate the environmental impact of pharmaceuticals in one way or another into the various bio-health degrees. It will also be necessary to continue to raise awareness and train all practitioners on this complex issue.

The University of the Basque Country recently conducted the first edition of the online postgraduate course entitled 'Titulo de Experto Universitario en Farmacontaminacion' (English translation: University Expert in Drug Pollution) focusing on the current problem of environmental pollution by drugs and potential solutions (https://www.ehu.eus/es/web/graduondokoak/experto-universidad-farmacontaminacion).

There is a clear need for collaboration and bridge-building between the healthcare and environmental worlds. The drug knowledge possessed by healthcare professionals can prove valuable in developing and implementing measures to address the problem, as well as in conducting research. An example is the assessment of the presence and environmental impact of hazardous medicines, led by hospital pharmacists.[56,57]

End-of-pipe

A complementary measure to all of the above would involve applying additional treatment to wastewater to improve the removal of pharmaceuticals, a concept known as 'end-of-pipe.'

Currently, wastewater treatment in most countries, including Spain, is not sufficient to remove pharmaceuticals. In addition, around half of the world's wastewater is not treated at all.[58] For more detailed information: https://www.hydrosheds.org/products/hydrowaste.

There are many methods that are available to help remove pharmaceuticals from wastewater, including advanced oxidation treatments (such as ozone and photocatalysis), separation techniques (such as membranes), adsorption, activated carbon, or a combination of these. The only country widely implementing advanced technology (i.e. ozone + activated carbon) is Switzerland, primarily due its high cost (detailed information at: https://micropoll.ch/fr/realisations-dans-les-step/).

Another strategy involves intervening in drug emission hotspots, such as hospitals, to reduce the volume of water requiring treatment, thereby lowering costs. For years, numerous public–private initiatives have been underway to install infrastructure aimed at improving hospital wastewater treatment, such as the one at Herlev Hospital in Copenhagen (https://ultraaqua.com/wp-content/uploads/2020/12/wastewater-treatment-at-herlev-hospital-denmark-ultraaqua.pdf). Hundreds of studies have been published on a variety of advanced hospital wastewater treatments to remove pharmaceuticals.[59] Several of these studies have been conducted in Spanish hospitals.[60]

Conclusions

The problem of environmental pollution by medicines is complex. So far, healthcare professionals have paid little attention to this issue. However, we are probably at a turning point that could prompt a paradigm shift in our profession, in which the environmental aspects of medicines will play a significant role. It is time to get moving.

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Declaration of competing interest

None declared.

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