A potential solution to reduce the pharmaceutical contamination of surface water with the ultimate objective of GHGs emission reduction

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Good Practice

On-site separate collection and treatment of human urine containing pharmaceutically active drug compounds before being drained to the sewage water streams could be a very promising approach to minimize the emergence of multi-drug resistance and various other associated hazards. It reduces the burden on centralized sewage water treatment plants (WTPs) which are mostly inefficient to effectively remove the pharmaceutically active contaminants from wastewater streams. Moreover, if WTPs are made to be more efficient or advanced, then the electricity use associated with pumping and treatment procedures would be significantly higher, and also the use of chemicals, resulting in a higher direct and/or indirect CO_2 emission. Hence, separate treatment measures for waste streams containing pharmaceutical compounds could be a more economical and eco-friendly approach to deal with this issue.

Case Summary

Indian Institute of Technology Patna is one of the second generation IITs established by an Act of the Indian Parliament on August 06, 2008. The Indian Institute of Technology Patna's

campus is located at Kanpa road, Bihta (about 35 km from Patna city). The institute is spread over a sprawling 203 hectare campus in an eco-friendly environment. It's a small self-sustaining town with about 2,200 inhabitants, including faculty members, students, staffs and other helping hands. The campus is well-equipped with state of the art academic cum research infrastructures and other essential facilities including residential buildings, recreational areas, shopping complexes and health care facilities. It also includes a dedicated sewage treatment plant with an estimated capacity of 250 m^3 per day and is based on MBBR (moving bed biofilm reactor) technology. The serviced population for this treatment plant is about 1500 persons, and the average energy consumption of this sewage treatment plant is about 120 kWh per day. Using WaCCliM project's ECAM (Energy performance and Carbon emissions Assessment and Monitoring) tool (v2.1 beta), the direct and indirect GHG emission is about 176.09 kg of CO_2 per day, where the major part of GHG emission is indirectly resulting from the electrical energy consumption, i.e, above 90% of total emission (please see **Fig. 1**). However, any sorts of special measure to treat any specific or persistent compounds such as pharmaceutical waste residues are not available with the existing sewage treatment system. Hence, the existing treatment system does not seem to be sufficient enough for the effective and/or efficient removal of pharmaceutically active compounds based pollutants, which are also known as the contaminants of emerging concern. To better understand the importance of this issue, readers are requested to go through the enlisted news articles reported in the last couple of years (please see **Table 1** in the appendix section). The detailed pharmacokinetics of pharmaceutical antibiotics, which were mainly consumed by the residents of IIT Patna campus in a specific time duration (as represented in **Fig. 2**), have also been reviewed (please see **Table 2** in the appendix section).

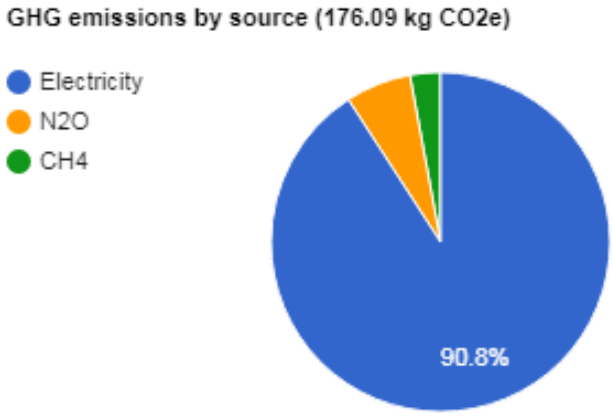

Fig. 1 Total GHG emission due to the operation of sewage treatment plant at IIT Patna campus (in a day, estimated with the help of ECAM tool).

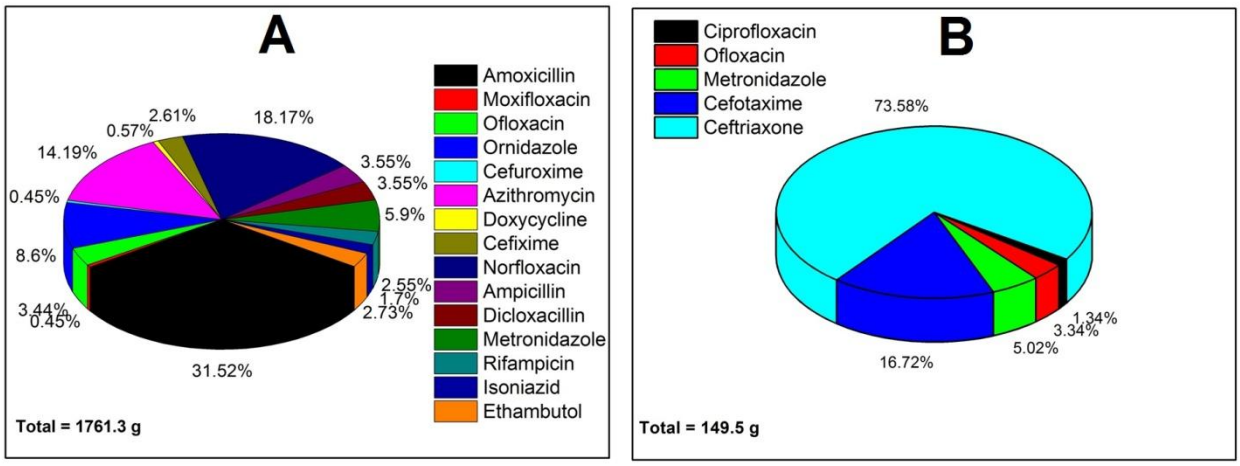

Fig. 2 Total antibiotic consumption in 2nd quarter of 2018 at IIT Patna campus: (**A**) Oral consumption; (**B**) Intravenous (IV) or intramuscular (IM) consumption.

In general, human urine is considered as a source of contamination due to the presence of nitrogen and phosphorous contents (if it is directly disposed to the open environment or receiving water bodies). Moreover, pharmaceutical traces present in the human urine used to cause further contamination of the eco-system, as the pharmacokinetics of pharmaceutical compounds suggest. The pharmaceutical metabolites that end up in human urine also make their way out into external waterways, with some unanticipated outcomes. Hence, the presence of pharmaceutical compounds such as antibiotics in the human urine should be considered as a radical source of water contamination that may also lead to the emergence of multi-drug resistance. It has already been testified that a huge part of administered drug used to excrete from the human body, especially through the human urine. The excretion level of administered drug through human urine has been estimated about 40-60% of its active dose, depending on the type of drug, its pharmacokinetics and pharmacodynamics parameters. That proportion may also increase further if the drug has been administered through an intravenous (IV) mode. Hence, the removal or degradation of these pharmaceutical compounds present in the urine or other real wastewater matrices mixed or contaminated with some patients' urine is a foremost necessity due to the frequent notifications of various multi-drug resistance based disease outbreaks in whole biosphere. Thus, these compounds are subsequently required to be removed from the urine matrix before their dissolution into the bulk or sewage wastewater streams. As a whole, the *ex-situ* handling and treatment of contaminated wastewater matrix mixed with urine containing pharmaceutical compounds used to be relatively more challenging and uneconomical than its *in-situ* treatment. Since, the *ex-situ* or centralized wastewater treatment facilities are quite inefficient and inadequate to remove the pharmaceutical waste via conventional wastewater treatment methodologies, the

pharmaceuticals and associated metabolites are continuously being discharged into the open water resources. Note that, human urine contributes less than 1% of the total volume processed in municipal wastewater treatment plants (Landry and Boyer 2016). Therefore, urine collection at source followed by *in-situ* or separate *ex-situ* treatment has been proposed to effectively treat a limited volume of concentrated pharmaceutical compounds present in a small batch. The additional benefit of this source separated urine treatment is the possibility of efficiently recovering nitrogen, phosphorus, and potassium based nutrients for their utilization as the eco-friendly fertilizer (Simha and Ganesapillai 2017). Besides this, it should also be noted that the separate collection and diversion of human urine is not a very new topic. People have already been using this process for agricultural benefits since a long time ago (Kvarnström et al. 2006). Moreover, some recent studies are also suggesting about the potential applicability of human urine as a promising energy source too (Gao et al. 2018; van der Hoek et al. 2016; Walter et al. 2017).

Background

Pharmaceutical compounds are considered as one of the greatest innovations, extensively being used for the betterment of human as well as other living organisms' health and illness. The pharmaceutical residues are found in raw water resources, and sometimes in very low concentrations in drinking water too (Boxall et al. 2012). Thus, the presence of these pharmaceutical compounds in the open environment has also become a subject of serious concern and debate due to their adverse effects on the biosphere (please see **Table 1** in the appendix section). Few examples of potential pharmaceutical contamination based risks are:

- Emergence of multi-drug resistance.
- Hormonal or endocrine disruption that may induce sex changes in fish and amphibians.
- The presence of a variety of drugs such as analgesics, antibiotics, anti-platelet agents, hormones, psychiatric drugs, antihistamines may imbalance the aquatic and terrestrial lives.

About 70 to 80% of all pharmaceuticals consumed by humans and farm animals that used to be about thousands of tons, end up into the natural environment, especially in surface water resources. As sewage water is a major source of contamination for almost all rivers around the globe, a large number of pharmaceutical compounds are being found at quite alarming

levels in these rivers. Moreover, if this situation continues for a longer duration, the pharmaceutical compounds present in surface water matrices may start to leach-out into groundwater or aquifers and cause the contamination at that level too. Thus, our fresh water resources are also under the potential risk of pharmaceutical contamination. In regions like Latin America, Africa and Asia, the pharmaceutical contamination levels are more likely to be at higher risk as advanced wastewater treatment facilities are not commonly available in various parts of these regions, and the available water treatment systems are not efficient enough to treat or filter-out most of the pharmaceuticals. Moreover, the retention time of wastewater matrices in the treatment plants is also used to be very short, which is not enough for the effective degradation or neutralization of many of pharmaceutical substances.

In the last few years, several studies revealed that the irresponsible disposal or dumping of drug waste is fueling various health problems. However, the contribution of pharmaceutical industries towards the pharmaceutical compound based pollution is quite insignificant, as the major contamination arises from the self-medication and excess-use of pharmaceuticals and personal care products by major fractions of the communities. Scientists associated with the WHO and NAS (National Academy of Sciences) have already warned about the future health crisis due to several antibiotic drug resistances. There is one quote from David Cameron (former UK Prime Minister), "*If we fail to act, we are looking at an almost unthinkable scenario where antibiotics no longer work and we are cast back into the dark ages of medicine*". Moreover, some reviews claim that drug-resistant infections alone could kill an extra 10 million people across the world every year by 2050, if they are not properly tackled. Continuous exposure of antibiotics (present in mixed wastewater streams, typically in lower concentrations) to the pathogenic bacterial cells provides an impetus in the development of multi-drug resistants from the normal pathogenic bacterial cells (Verma and Samanta 2016). These multi-drug resistant strains are very difficult to treat with the routine medical treatment protocols. Consequently, it requires some additional medical efforts and advanced generation drugs for an effective medical treatment that eventually increase the overall cost of medical treatment as well. Moreover, even after the incorporation of advanced medical treatment facilities the results of the medical treatment used to be quite uncertain in the term of success. Therefore, we need proper handling and disposal of pharmaceutical wastes.

In India, these parameters are handled as per wastewater discharge guidelines prescribed by the Central Pollution Control Board (CPCB). Unfortunately, the latest standards do not consider pharmaceutical traces or residues, hence, they are not being properly monitored and

treated in effluent resources. Besides this, the need of wastewater discharge guidelines to be stringent on the urgent basis could be perceived from the statement that– Indian pharmaceutical industries are the fastest growing segment of the Indian economy that globally contributes about 80% of drug production, alongside China.

Proposed Solution

Various advanced oxidation processes (AOPs), adsorption or filtration based processes (such as granular activated carbon (GAC), powdered activated carbon (PAC) and membranes), and their combinations like ozone–GAC have potential to be used for the effective removal and/or the degradation of pharmaceutical pollutants present in urine or wastewater matrices. Here, processes other than AOPs involve the separation of pharmaceuticals from one phase to another, and they do not offer the degradation of pharmaceuticals; whereas the electrical energy consumption cost associated with the AOPs used to be extremely high (Verma and Samanta 2018; Chong et al. 2012). Therefore, usage of AOPs at full scale water treatment plants used to be very uneconomical that also significantly increases the GHGs emission, as estimated via ECAM tool. Hence, selective and needful usage of AOPs for limited wastewater matrices is highly recommended. For the same, a separate collection of human urine followed by the treatment via AOPs has been considered as an obvious necessity. In this regard, we propose two different urinal layouts depending on the treatment volume or population load, infrastructure and resource availability in the region (such as energy and its cost). These urinal layouts are as follows:

- **Layout A** involves the connection of all urinal systems to the AOPs directly without any segregation or visual distinction of the urinals. This makes the system very uniform for all the users, and there would be no scope of discrimination or confusion among the users. However, in this layout, we need to treat all urine through AOPs that would be slightly uneconomical in the developing nations with high population density and low energy resources such as India, Bangladesh, Pakistan and Latin America.
- **Layout B** involves a color based urinal system that could be effectively utilized to cope with the limitation of Layout A. This layout has one (or more) dedicated-red-colored urinal for separate collection of urines containing pharmaceuticals followed by AOP based treatment. Although this layout offers quite low treatment volume through energy intensive AOPs, this system may become vulnerable if some users

choose the wrong urinal, which is quite expected during public usage. Hence, the awareness among the users and their attentiveness may play a very crucial role in the success of this proposed layout.

These proposed layouts of the urinal system (please see **Fig. 3**) could be effectively utilized based on demographic distribution and economic condition of the region (as discussed earlier), and may significantly prevent the spreading of pharmaceutical residues in the open aquatic environment.

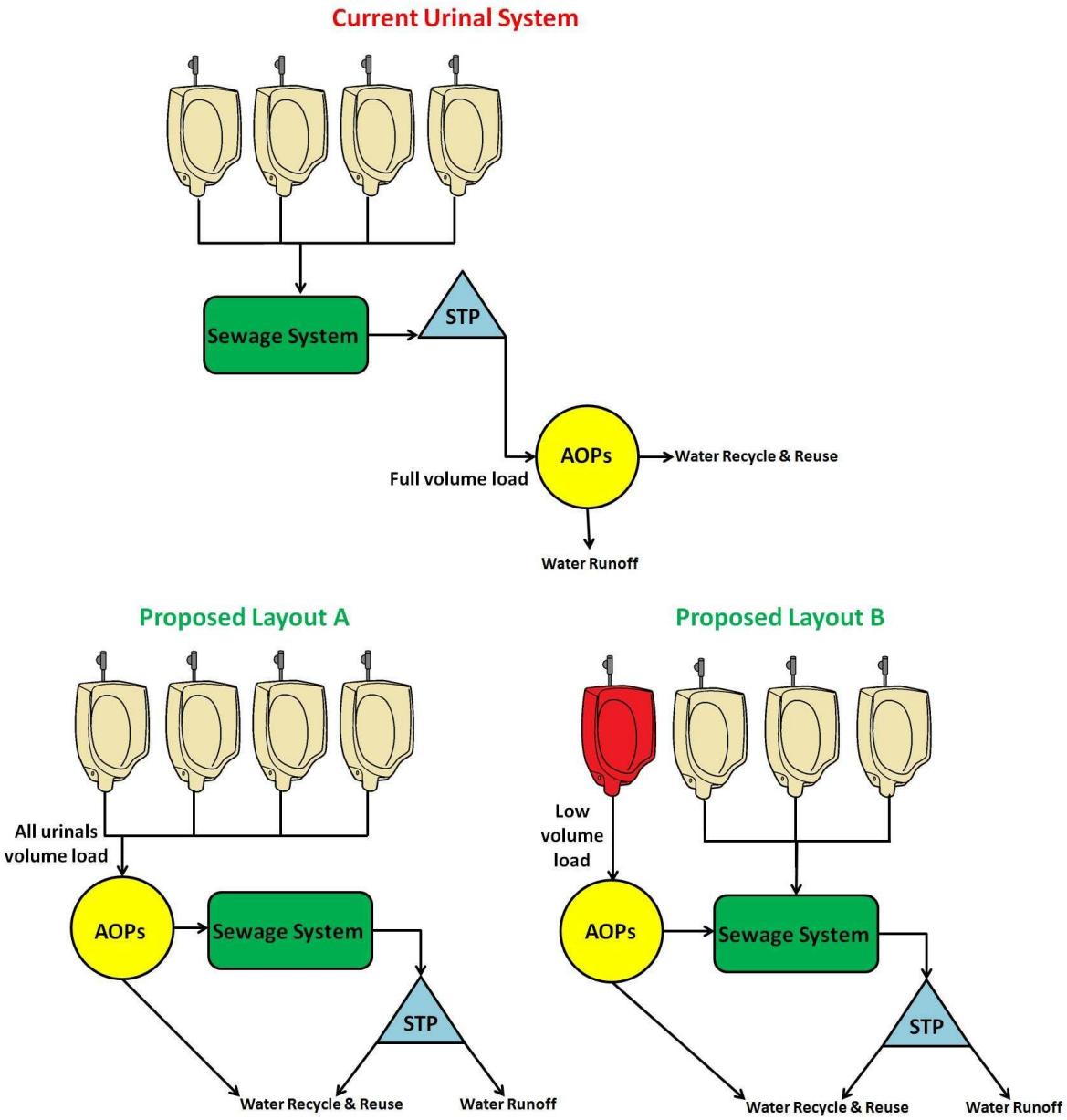

Fig. 3 Schematic of the existing urinal system, and proposed layouts (**A** and **B**).

Challenges

There is a discrepancy in the production of drugs and their ultimate utilization. It has been observed that most of the developing nations do not lack the infrastructure for pharmaceutical waste management. The major problem is the lack of awareness among the communities who dispose the used or unused pharmaceuticals and related waste along with general waste. Typically, that kind of waste is finally burnt or thrown in landfills. Either way, it becomes highly hazardous when it comes in contact with the water bodies and the atmosphere. It enters the food chain and affects minors and aged people as they are the most vulnerable due to their lower immunity. In routine practice, the pharmaceutical wastes are largely destroyed at very high temperatures (~1,200°C), that require some special kind of incinerators to achieve this temperature. However, the adequate control over emissions and huge energy cost are still the major concerns for economical and eco-friendly usage of these incinerators. Generally, antibiotics, anti-cancer drugs, disinfectants and non-biodegradable compounds should not be disposed into the sewage system as they may kill the bacteria and other micro-organisms essential for the treatment of sewage influent (Basnyat 2011). However, due to the progressive dilution of sewage streams, this short term effect is used to be very limited and the major concern would be the long term outcomes such as the emergence of multi-drug resistance. Hence, on-site separate collection and treatment of human urine containing pharmaceutically active drug compounds (before being drained to sewage water streams) is quite obligatory.

The major challenge in the initial stage of the proposed methodology is the requirement of re-designing of urinal systems and installation of separate collection and treatment modules for effective and efficient treatment of pharmaceutically contaminated urine. Initially, it would require a huge capital cost which is quite difficult to be arranged in developing and underdeveloped nations, where food security and water scarcity are still much bigger issues. Furthermore, the power consumption or electricity cost optimization of the treatment procedures is also equally important during the application of this solution. Hence, special guidance and assistance of some field experts and dedicated organizations (such as WaCCliM) are also needed in this direction. In addition, to decide about the numbers of separate urinal installations on specific sites, it is required to have some previous usage data of existing urinals, so that the optimum number of dedicated urinal system could be effectively estimated for the future installations. Besides this, the proper awareness of the functionality or utility of these dedicated urinals among the common people or end-users is

also a big challenge, especially in developing and underdeveloped nations where literacy rate is quite low.

Activities

There are various national and international funding resources and NGOs that could be approached for needed funds, related to the installation of dedicated urinal and treatment system to cope with the pharmaceutical waste present in human urine.

Moreover, for optimization of the contaminated urine treatment procedures, WaCCliM approach could help in a tremendous manner. It provides an Energy performance and Carbon emissions Assessment and Monitoring (ECAM) tool that could be conveniently utilized for various baseline assessments such as identification of all direct and indirect sources of carbon dioxide (CO_2), methane (CH_4) and nitrous oxide (N_2O) emissions in all the stages of the contaminated urine collection, treatment, and reuse or discharge train followed by nutrient and/or energy recovery. It will effectively reduce the energy consumption and GHG emission by applying various energy optimization measures on pumps and treatment processes involved in the urine treatment train system.

At the same time, there is also a potential scope of utilization of treated urine as a source of nutrient for cultivation and growth of microorganisms producing metabolites with commercial values, biogas, and electricity production via microbial fuel cells based techniques. Moreover, the recovered urea, phosphorus and nitrogen from the treated urine could be used as the green source of fertilizer for agriculture. The combination of urine treatment with the energy and nutrient production methodologies would result in a substantial reduction of kWh units of energy and cost of treatment per m^3 of treated urine. In this regard, the knowledge platform of WaCCliM project has very propitious potential to offer an energy-positive recovery of nutrients from urine, avoiding energy-intensive and complicated processes in urine handling and nutrient removal during contaminated urine treatment, and may also offer various better ways for the storage and reuse of urine. Overall, the incorporation of WaCCliM approaches could considerably help in the economic and the green structuring of sustainable ways for the water–nutrient–energy nexus. Above all, the induction of some awareness programs in public places, advertisements on print and electronic media, etc. may help to educate and better spread awareness among the common people or end-users regarding this subject.

Institutions Involved or Key Players

The WaCCliM project, which aims to reduce the carbon footprints of water and wastewater utilities, has inspired to work on this strategy. The WaCCliM project is implemented by the Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ), the International Water Association (IWA) and their local partner the National Water Commission (CONAGUA), on behalf of the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU) as part of the International Climate Initiative (IKI).

The tool developed under WaCCliM project, namely ECAM (Energy performance and Carbon emissions Assessment and Monitoring) tool (v2.1 beta) has substantially helped us to have a better estimation about the major sources and cause of GHG emissions involved in the process (http://wacclim.org/ecam-tool/). In addition, it adequately helps us to take a decision about the optimal processing of contaminated human urine with reduced electrical energy cost, and so reduce the GHG emissions too.

In Cooperation With

The research facilities provided by the Indian Institute of Technology Patna have significantly helped us to establish and conclude about the promising solutions that could be appropriately used for the treatment of pharmaceutically contaminated urine, and nutrients' recovery for additional benefits.

Financing

In India, Ministry of Environment, Forest and Climate Change, Government of India (GoI) used to provide funds in various schemes such as National River Conservation Programme (NRCP), National Lake Conservation Plan (NLCP), National Plan for Conservation of Aquatic Eco-systems (NPCA). In general, the financial assistances are provided to the state governments for conservation of identified water resources in the country, on cost sharing basis (between the central government and respective state governments). In addition, this ministry also provides grants to the State Pollution Control Boards (SPCBs) or Pollution Control Committees (PCCs), Environment Departments of States, Central or State Research Institutes and other Government agencies/organizations under the scheme of 'Assistance for Abatement of Pollution'. Moreover, central subsidy is also provided by this ministry to state governments for establishment of Common Effluent Treatment Plants (CETPs). We believe that, the CETPs would be the most suitable category to apply for the funds required for the

development of separate advanced oxidation treatment plant for effective and economic treatment of contaminated human urine and nutrient recovery.

However, to access the funds under these GoI schemes require submitting the project proposals under a suitable category of available schemes. Afterwards, the responsible divisions will scrutinize the submitted projects, check the suitability of terms and conditions, and allocate the funds to competent projects. Unfortunately, not all submitted projects are approved due to the large number of applications and limited budget availability under these schemes.

Mode of Application: "The complete application indicating the requirements, list of equipments (if any), along with the objectives, justification, budgets and in case of short studies the need for undertaking such studies as well as utilization of output towards abatement of pollution may be sent to the Director (CP), Ministry of Environment and Forests, New Delhi 110003" (http://www.moef.nic.in/public-information/funding-schemes).

Impacts

This strategy provides a simultaneous solution for two major issues related to the conventional wastewater treatment plants: first is their inefficiency to handle pharmaceutical waste; and second is the requirement of huge energy and technology based inputs for handling a large volume of treatment matrix via AOPs at tertiary treatment level. The incorporation of advanced oxidation technologies in conventional wastewater treatment plants has potential to deal with those pharmaceutical contaminants. But, the incorporation of AOPs at full-scaled conventional water treatment plants requires huge energy inputs (as it requires to handle a large volume of feed or influent that may increase the pumping cost, treatment cost, and other associated costs depending on the treatment volume) and could not become a sustainable choice for future development. Typically, advanced oxidation based treatment procedures used to be the most prominent solution for the implementation of measures to improve the treatment outputs, but at the same time they are quite uneconomical too. Hence, the on-site separate collection and treatment of human urine (containing pharmaceutically active drug compounds) could effectively reduce the burden on centralized wastewater treatment plants which are mostly inefficient to effectively remove the pharmaceutical compounds from mixed wastewater streams. In addition, it will significantly reduce the volume of the pharmaceutically active compound-contaminated waste matrix that requires advanced treatment procedures.

Furtherance in the directions of nutrient and energy recovery from the treated waste matrix via various developing technologies is also quite realizable. This step would further decrease the GHG emissions in three different ways: first, the nitrogen still present in the treated matrix would be used as a fertilizer rather than being partially transformed into N_2O in the surface water bodies; second, the nitrogen obtained via this method would offset the other commercial fertilizer requirements and thereby reduce the associated emission related to the fertilizers' manufacturing [For example: Ammonia synthesis via Haber–Bosch process for nitrogen-based fertilizers production alone consumes about 1% of global energy (Palys et al. 2018)] and transportation too; and third, the produced energy from the microbial fuel cell technology may reduce the electricity consumption (at least up to some extent).

Success Factors

There is an urgent need to implement stringent guidelines for treatment and monitoring of waste discharged from pharmaceutical industries, hospitals, medical dispensaries and health centers. Moreover, it should also be considered and/or acknowledged that the conventional wastewater treatment plants are not adequately equipped with the treatment facilities which are essential for effective removal of pharmaceutical contaminants from the discharged streams.

To make the solution globally successful, first of all, the researchers, governments and global communities need to consider and scrutinize some major concerns related to the presence of pharmaceuticals and personal care products (PPCPs) in the environment, before going for any solid conclusive remarks related to the usage and disposal of pharmaceutical compounds and their waste. The concerns represented here, were mainly proposed by Boxall et al. (2012) for pharmaceuticals and personal care products' presence in the open environment; where the major concerns were selected through the experts voting at an international expert workshop. However, only the most recognized concerns with more than 30% votes are mentioned here. These major concerns are as follows: "(**1**) How important are pharmaceuticals and personal care products relative to other chemicals and nonchemical stressors in terms of biological impacts in the natural environment?; (**2**) What approaches should be used to prioritize pharmaceuticals and personal care products for research on environmental and human health exposure and effects?; (**3**) Does environmental exposure to pharmaceuticals and personal care products residues result in the selection of antimicrobial resistant microorganisms, and is this important in terms of human health outcomes?; (**4**) How can ecotoxicological responses, such

as histological and molecular-level responses observed for pharmaceuticals and personal care products, be translated into traditional ecologically important end points such as survival, growth, and reproduction of a species?; (**5**) How can pharmaceutical preclinical and clinical information be used to assess the potential for adverse environmental impacts of pharmaceuticals?; (**6**) What can be learned about the evolutionary conservation of PPCP targets across species and life stages in the context of potential adverse outcomes and effects?; (**7**) How can effects from long-term exposure to low concentrations of PPCP mixtures on non-target organisms be assessed?".

Awareness, engagement and interest of global communities and stakeholders towards the solution of this emerging critical issue would decide the success of the given methodology. However, it is too early to consider about the success of the proposed solution as most of the things are lagging at their implementation level. Hence, some more time and intensive efforts are needed to exactly comment about the success factor of this methodology. Besides this, the incorporation of this solution may also provide some job opportunities too, as a significant man power is presumed to be required at the initial and the operational stages of the proposed solution.

Obstacles Overcome

The main barrier to overcome is the limited awareness of this issue in common public communities that needs to be ameliorated at global level. Global communities need to understand that it is not just about the disposal of urine, but the safe disposal of pharmaceutical contaminants present in the urine. It should also be realized that more harmful effects could emerge from the substandard pharmaceutical waste treatment and management system.

As per economical and technical perspective, the initial costs associated with the advancement of existing urinal systems and add-on of the microbial fuel cells based energy recovery systems are very unendurable. In addition, the routine maintenance is also very exigent for nutrient and energy recovery processes. Hence, various energy recovery based techniques are required to be further developed in this direction.

Lessons Learned

Separate urine treatment systems with pilot scale would have a lower environmental impact than the full scale or centralized cum hybrid wastewater treatment plants. Overall, it has also

been perceived that the technology alone could not solve this problem. Communities or end-users also need to understand their responsibilities towards the sustainability of a green and healthy environment.

The present regulations and laws are still needed to be strengthened to introduce proper environmental standards. These regulations should ensure to put very stringent limits on the presence of any pharmaceutically active compounds in effluents. Minor and lower budget establishments must be supported by the governmental and non-governmental organizations for the installation and implementation of proposed solutions related to the treatment and disposal of pharmaceutically contaminated human urine matrices. In addition, the high-end sewage treatment plants must be strictly monitored, and concerned regional authorities such as state/city pollution control boards should conduct surveillance of pharmaceutical residues in those treatment plants' effluent. Moreover, the collected data should be made publicly available in order to spread the awareness around that region.

Replication

These are some major factors which are very essential for the replication of this methodology:

- Surveillance of pharmaceutical residues, associated toxicities and multi-drug resistance in the environment, including industrial, hospital, public places, and municipal water discharges.
- Standards for pharmaceutical waste residues in effluent streams.
- Environmental risk assessment for various related establishments.
- Provisions for legislation, awareness and incentives related to this issue.
- Training of communities and end-users for the effective and efficient usage of treatment solutions.

The Best Practice

The adaptation of the proposed layout either involving connection of all urinal systems to the AOPs first or disintegration of the existing urinal system into two categories (one for normal urine, connected to the sewage system; and another for pharmaceutically contaminated urine, connected to the AOPs) is a best practice for long term sustainability of the effective separation, removal or degradation of pharmaceutical contaminants present in human urine.

This is a best practice example, as both utilities fully completed the WaCCliM Roadmap cycle approach to achieve both pollutant and GHG emission reductions, and have the potential to become a climate mitigation trend-setter in the utilized regions. Overall, this case study may enable us to pave the way for a sustainable water–nutrient–energy nexus.

The Next Steps

Government and public authorities need to install separate urinals for those persons who have been receiving some kind of pharmaceutical treatments either in the form of oral or in the form of injectable drugs. Ideally, for a developing nation like India (which is very densely populated), one dedicated urinal for every 3 or 4 normal urinals could be an optimum ratio for initial development in this direction. At the same time, the government or policy makers also need to spread awareness among the common people or end-users regarding the concerns and objectives related to the urinal categorization, marking, and their appropriate usage. Further via continuous monitoring of the usage of these dedicated urinals in specific places, the authorities would be able to assess the requirement of additional dedicated urinals' installation at monitored sites. In the future, the government or policy makers may also look forward to install similar dedicated urinals in public transport system such as long route trains, buses, and planes.

Quotation

As we know that:

What is not observed cannot be investigated;

What is not investigated cannot be changed;

What is not changed cannot be improved, and we are on that stage regarding this issue.

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Appendix

Table 1. The list of some alarming articles related to the pharmaceutical waste and their negative outcomes.

S. No.	Titles of public news articles	Link or Resource
1	Fears grow over increased antibiotic resistance (16 October 2015)	http://www.bbc.com/news/health-34541253
2	Antibiotic resistance: World on cusp of 'post-antibiotic era' (19 November 2015)	http://www.bbc.com/news/health-34857015
3	Antibiotic resistance	http://www.sciencedaily.com/terms/antibiotic_resistance.htm
4	Antibiotic resistance rise continues (10 October 2014)	http://www.bbc.com/news/health-29553435
5	Analysis: Antibiotic apocalypse (19 November 2015)	http://www.bbc.com/news/health-21702647
6	Antibiotic 'apocalypse' warning (24 January 2013)	http://www.bbc.com/news/health-21178718
7	Antibiotic resistance now 'global threat', WHO warns (30 April 2014)	http://www.bbc.com/news/health-27204988
8	Antibiotic resistance: What is a superbug? (19 November 2015)	http://www.bbc.com/news/health-34870972
9	Q&A: Antibiotic resistance (19 November 2015)	http://www.bbc.com/news/health-21739378
10	Antibiotics: Are we reckless drivers when it comes to drugs? (18 August 2015)	http://www.bbc.com/news/health-33963353
11	Antibiotics: US discovery labelled 'game-changer' for medicine (7 January 2015)	http://www.bbc.com/news/health-30657486
12	Most countries not protecting antibiotics, says WHO (29 April 2015)	http://www.bbc.com/news/health-32515967
13	Call for $2bn global antibiotic research fund (14 May 2015)	http://www.bbc.com/news/health-32701896
14	Antibiotic resistance: 80,000 'might die' in future outbreak (6 April 2015)	http://www.bbc.com/news/uk-32193606
15	Antibiotics resistance 'as big a risk as terrorism'-medical chief (11 March 2013)	http://www.bbc.com/news/health-21737844
16	The drugs don't work - so what will? (9 April 2011)	http://www.bbc.com/news/health-13005739
17	Europe 'losing' superbugs battle (7 April 2011)	http://www.bbc.com/news/health-12975693
18	Viewpoints: Finding new antibiotics (2 July 2014)	http://www.bbc.com/news/health-28116565
19	Antibiotic resistance 'big threat to health' (16 November 2012)	http://www.bbc.com/news/health-20354536
20	Gonorrhoea strain found to be 'resistant to antibiotics' (11 July 11)	http://www.bbc.co.uk/news/mobile/health-14078098
21	DNA sequencing of MRSA used to stop outbreak (14 November 2012)	http://www.bbc.com/news/health-20314024
22	'Golden age' of antibiotics 'set to end' (8 January 2014)	http://www.bbc.com/news/health-25654112
23	GPs 'over-prescribing' antibiotics, says Cardiff University study (23 October 2013)	http://www.bbc.com/news/uk-wales-24644191
24	Cardiff University-led team finds New Delhi water bug (7 April 2011)	http://www.bbc.com/news/uk-wales-south-east-wales-12989782
25	New 'superbug' found in UK hospitals (11 August 2010)	http://www.bbc.com/news/health-10925411
26	Q&A: NDM-1 superbugs (11 August 2010)	http://www.bbc.com/news/health-10930031
27	Study into resistant Midlands superbugs (1 April 2010)	http://news.bbc.co.uk/2/mobile/uk_news/england/west_midlands/8597851.stm
28	Battling the bacterial threat to modern medicine (30 November 2012)	http://www.bbc.com/news/health-20554921
29	Fears over risk of air transmission of superbugs (11 October 2012)	http://www.bbc.com/news/health-19898735
30	Doctors 'should snoop on antibiotic prescribing' (18 February 2015)	http://www.bbc.com/news/health-31490652
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32	Are we losing the fight against superbugs? (9 November 2011)	http://www.bbc.com/news/uk-15650031
33	India rejects UK scientists' 'superbug' claim (12 August 10)	http://www.bbc.co.uk/news/mobile/world-south-asia-10954890
34	Superbugs to kill 'more than cancer' by 2050 (11 December 2014)	www.bbc.com/news/health-30416844
35	Roche pulls out of "superbug" antibiotic project (29 November 2015)	http://in.reuters.com/article/2015/11/29/roche-antibiotics-idINKBN0TI0PJ20151129
36	Doctors urged to cut medicine prescription waste (22 July 2013)	https://www.bbc.com/news/health-23374000
37	Drug waste clogs rivers around the world, scientists say (11 Apr 2018)	https://www.theguardian.com/environment/2018/apr/11/drug-waste-clogs-rivers-around-the-world-scientists-say
38	One bag of wasted medicines worth a week in the Bahamas (30 Jun 2016)	https://www.rpharms.com/news/details/One-bag-of-wasted-medicines-worth-a-week-in-the-Bahamas
39	Big Pharma's pollution is creating deadly superbugs while the world looks the other way (06 May 2017)	https://www.thebureauinvestigates.com/stories/2017-05-06/big-pharmas-pollution-is-creating-deadly-superbugs-while-the-world-looks-the-other-way
40	Need stringent guidelines for treatment of pharmaceutical waste: Experts (20 May 2018)	https://www.business-standard.com/article/pti-stories/need-stringent-guidelines-for-treatment-of-pharmaceutical-waste-experts-118052000176_1.html https://www.indiatoday.in/pti-feed/story/need-stringent-guidelines-for-treatment-of-pharmaceutical-waste-experts-1237237-2018-05-20 https://www.moneycontrol.com/news/business/need-stringent-guidelines-for-treatment-of-pharmaceutical-waste-experts-2571851.html
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42	Impacts of pharmaceutical pollution on communities and environment in India (01 February 2016)	http://www.indiaenvironmentportal.org.in/content/428018/impacts-of-pharmaceutical-pollution-on-communities-and-environment-in-india/
43	Pharmaceuticals in drinking-water (01 August 2012)	http://www.indiaenvironmentportal.org.in/content/360454/pharmaceuticals-in-drinking-water/
44	Improper disposal of pharmaceutical waste continues to be a problem (20 May 2017)	https://www.thehindu.com/news/cities/bangalore/improper-disposal-of-pharmaceutical-waste-continues-to-be-a-problem/article18517180.ece
45	Dangers of poor pharmaceutical waste disposal (07 December 2017)	https://www.businessdailyafrica.com/news/Danger-poor-pharmaceutical-waste-disposal/539546-4218120-yy1mtr/index.html
46	Updates and Tips for Pharmaceutical Waste Management (3 October 2017)	https://www.pharmacypracticenews.com/Review-Articles/Article/10-17/Updates-and-Tips-for-Pharmaceutical-Waste-Management/44700
47	Treating Pharmaceutical Waste	https://noharm-global.org/issues/global/treating-pharmaceutical-waste
48	What happens to the excreted drugs you flush down the toilet? (8 August 2014)	https://www.theguardian.com/science/blog/2014/aug/08/drugs-toilet-pharmaceutical-pollution
49	What about all the pharmaceuticals excreted in urine.	https://greywateraction.org/faq/what-about-all-the-pharmaceuticals-excreted-in-urine/
50	How drugs are entering UK water systems through urine (12 September 2014)	https://www.bbc.com/news/health-29108330

Table 2. The detailed pharmacokinetics of pharmaceutical antibiotics, mainly consumed inside the IIT Patna campus during 2nd quarter of year 2018 (April–June, 2018).

Antibiotic	Absorption/ Bioavailability	Volume of distribution	Protein binding	Metabolism	Route of elimination	Half-life	Clearance
Ceftriaxone	Not Available	5.78–13.5 L	95%	Negligible: Hepatic and gut flora metabolism.	33–67% in the urine.	5.8–8.7 h	0.58–1.45 L/h
Cefotaxime	Rapidly absorbed	-		Hepatic	20–36% in the urine (15–25% as the desacetyl derivative, the major metabolite)	~ 1h	-
Metronidazole	80% (by mouth), 60–80% (rectal), 20–25% (vaginal).	-	20%	Hepatic metabolism by hydroxylation, oxidation, and glucuronidation.	77% in the urine and 14% in feces as unchanged drug and metabolites within 5 days.	6–8 h	-
Ofloxacin	Bioavailability of ofloxacin in the tablet formulation is approximately 98%	-	32%	Hepatic	Elimination is mainly by renal excretion. About 65–80% of an administered oral dose of ofloxacin is excreted unchanged via the kidneys within 48 h of dosing. Four to eight percent of an ofloxacin dose is excreted in the feces. This indicates a small degree of biliary excretion of ofloxacin.	9 h	Not Available

Ciprofloxacin	Rapidly and well absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability is approximately 70% with no substantial loss by first pass metabolism.	-	20–40%	Hepatic. Four metabolites have been identified in human urine which together account for approximately 15% of an oral dose. The metabolites have antimicrobial activity, but are less active than unchanged ciprofloxacin.	Approximately 40–50% of an orally administered dose is excreted in the urine as unchanged drug.	4 h	Renal clearance = 300 mL/min
Amoxicillin	Rapidly absorbed after oral administration. 95% by mouth	-	~20% (in blood serum)	Hepatic metabolism accounts for less than 30% of the biotransformation of most penicillins	Most of the amoxicillin is excreted unchanged in the urine; its excretion can be delayed by the concurrent administration of probenecid. Approximately 60% of an orally administered dose of amoxicillin is excreted in the urine within 6–8 h.	61.3 min	Not Available
Norfloxacin	Rapid 30–40%	-	10–15%	Via liver and kidney	Following oral administration of a single 400 mg dose of norfloxacin in adults with normal renal function, approximately 25–40% of the dose is excreted in urine as unchanged drug and 5–10% as metabolites within 24–48 h, and at least 30% (range: 10–50%) is excreted in feces within 48 h.	3–4 h	~275 mL/min
Azithromycin	Bioavailability is 37% following oral administration.	31.1 L/kg	-	Hepatic. In vitro and in vivo studies to assess the metabolism of azithromycin have not been performed.	Biliary excretion of azithromycin, predominantly as unchanged drug, is a major route of elimination.	68 h; 11–14 h (for single dose), 68 h (for multiple dose)	Apparent plasma clearance = 630 mL/min (following single 500 mg oral and IV doses)

Dicloxacillin	Absorption of the isoxazolyl penicillins after oral administration is rapid but incomplete: peak blood levels are achieved in 1–1.5 h. Oral absorption of cloxacillin, dicloxacillin, oxacillin and nafcillin is delayed when the drugs are administered after meals. 60–80%	-	98%	Metabolized only partially	Dicloxacillin sodium is rapidly excreted as an unchanged drug in the urine by glomerular filtration and active tubular secretion. The drug is also partly excreted in feces via biliary elimination. Following the oral administration of a single 250 mg, 500 mg, or 1 g dose of dicloxacillin in adults with normal renal function, 31-65% of the dose is excreted in urine as an unchanged drug and active metabolites within 6–8 h; approximately 10–20% of this is the active metabolite.	0.7 h	Not Available
Ampicillin	62±17% (parenteral) < 30–55% (oral)	-	15–25%	12–50% metabolites to penicilloic acid.	Ampicillin is excreted largely unchanged in the urine. 75–85% renal.	~1h	Not Available
Cefixime	About 40–50% absorbed orally whether administered with or without food, however, time to maximal absorption is increased approximately 0.8 h when administered with food. 30–50%	-	~60%	Hepatic.	Approximately 50% of the absorbed dose excreted as unchanged in the urine in 24 h.	3–4 h (may range up to 9 h). In severe renal impairment (5–20 mL/min creatinine clearance), the half-life increased to an average of 11.5 h.	Not Available

Ethambutol	About 75–80% of an orally administered dose of ethambutol is absorbed from the gastrointestinal tract.	-	20–30%	Hepatic. Up to 15% of administered drug is metabolized to inactive metabolites. The main path of metabolism appears to be an initial oxidation of alcohol to an aldehydic intermediate, followed by conversion to a dicarboxylic acid.	During the first 24h, following the oral administration of ethambutol hydrochloride, approximately 50% of the initial dose is excreted unchanged in the urine, while an additional 8–15% appears in the form of metabolites. From 20–22% of the initial dose is excreted in the feces as an unchanged drug.	3–4 h for normal renal function; Up to 8 h for impaired renal function.	Not Available
Rifampicin	Well absorbed from the gastrointestinal tract. 90–95% (by mouth)	-	89%	Primarily hepatic, rapidly deacetylated.	Less than 30% of the dose is excreted in the urine as rifampin or metabolites. Urine (~30%), faeces (60–65%)	3.35±0.66 h	0.19±0.06 L/h/kg (300 mg IV); 0.14±0.03 L/h/kg (600 mg IV)
Isoniazid	Readily absorbed following oral administration; however, absorption and bioavailability are reduced when isoniazid is administered with food.	-	Very low (0–10%)	Primarily hepatic. Isoniazid is acetylated by N-acetyl transferase to N-acetylisoniazid; it is then biotransformed to isonicotinic acid and monoacetylhydrazine.	From 50–70% of a dose of isoniazid is excreted in the urine within 24 h.	Fast acetylators: 0.5–1.6 h. Slow acetylators: 2–5 h.	-
Doxycycline	Completely absorbed following oral administration.	-	>90%	Hepatic	They are concentrated by the liver in the bile and excreted in the urine and feces at high concentrations in a biologically active form. In patients with normal renal function, approximately 20–26% of a single oral or IV dose of doxycycline is excreted in urine and 20–40% is excreted in feces within 48 h as an active drug.	18–22 h	-

Cefuroxime	Absorbed from the gastrointestinal tract. Absorption is greater when taken after food (absolute bioavailability increases from 37–52%).	-	50% to serum protein	The axetil moiety is metabolized to acetaldehyde and acetic acid.	Cefuroxime is excreted unchanged in the urine; in adults, approximately 50% of the administered dose is recovered in the urine within 12 h.	Approximately 80 min following the intramuscular or intravenous injection.	Not Available
Moxifloxacin	Well absorbed from the gastrointestinal tract. Absolute oral bioavailability is approximately 90%. Food has little effect on absorption.	1.7–2.7 L/kg	50% bound to serum proteins, independent of drug concentration	Approximately 52% or oral or intravenous dose is metabolized via glucuronide and sulphate conjugation. The cytochrome P450 system is not involved in metabolism. The sulphate conjugate accounts for 38% of the dose, and the glucuronide conjugate accounts for 14% of the dose.	Approximately 45% of an oral or intravenous dose of moxifloxacin is excreted as unchanged drug (~20% in urine and ~25% in feces).	11.5–15.6 h (for single oral dose)	12±2 L/h
Data resources: DrugBank and PubChem. "-" = Not found.							