

FATE AND REMOVAL OF PHARMACEUTICAL COMPOUNDS IN MEMBRANE BIOREACTOR

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by

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CERTIFICATE

This is to certify that the thesis entitled “Fate and Removal of Pharmaceutical Compounds in Membrane Bioreactor”, being submitted by Mr. Ashish Sengar, to the Indian Institute of Technology Delhi for the award of ‘Doctor of Philosophy’ in Department of Civil Engineering is a record of the bonafide research work carried out by him under my supervision and guidance. He has fulfilled the requirements for the submission of this thesis, which to the best of my knowledge has reached the requisite standard.

The material contained in the thesis has not been submitted in part or full to any other University or Institute for the award of any other degree or diploma.



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ABSTRACT

The release of pharmaceuticals in environmental waters has become an urgent issue due to their pseudo-persistent traits and damage they inflict on aquatic life. The major route by which pharmaceuticals enter environment is through wastewater treatment plant (WWTP) effluent discharge. With high self-medication rates, partial wastewater treatment coverage, and India being a pharmaceutical manufacturing hub, the contamination of Indian environmental waters with pharmaceuticals is severe. Despite numerous occurrence studies of pharmaceuticals in environmental waters of India, a comprehensive risk assessment study was still lacking. Amongst pharmaceuticals, iodinated X-ray contrast media (ICM) is a class of pharmaceuticals used in high quantities in medical examinations for organ imaging purposes. WWTPs have shown incapability to degrade ICM, and disinfection of ICM containing waters has shown to form highly cytotoxic and genotoxic iodinated disinfection byproducts. Despite several degradation studies on other pharmaceutical classes, ICM remains as least investigated. Considering these reasons, the present study has focused on evaluating a complete risk profile of India from the presence of pharmaceuticals in different environmental waters, and studied the fate of a recalcitrant pharmaceutical class- ICM in a lab-scale membrane bioreactor (MBR). This study was also extended to assess the fate of ICM in a lab-scale photocatalytic membrane reactor (PMR), hence mapping their complete fate in a secondary (MBR) and tertiary (PMR) treatment stage of a typical WWTP operation.

This study calculates the risk for human health, antimicrobial resistance (AMR) selection, and aquatic life due to the presence of a wide variety of pharmaceuticals in environmental waters. The study also analyzed the risk from the presence of personal care products (PCPs) in Indian environmental waters to picture the contamination of Indian water matrices from emerging

contaminants as a whole. The results of this study indicated that almost half of the detected pharmaceuticals and personal care products (PPCPs) (out of 98) in Indian environmental waters were found to exert a possible risk (risk quotient, $RQ > 1$) to either aquatic species, human health, or cause AMR selection risk.

MBR is an advanced biological treatment technology which has shown promising results in putting a barrier against the release of pharmaceuticals in environment owing to its potential of having a high solids retention time (SRT) and mixed liquor suspended solids (MLSS) concentration. Therefore, the present study has studied the fate of three ICM (iohexol, iopromide, iopamidol) in the long-term operation of a lab-scale MBR system, and also observed their effects on the performance of the MBR.

This study found that the presence of the ICM can aggravate the fouling in the MBR by causing changes in the sludge characteristics such as enhanced secretion of extracellular polymeric substances (EPS) ($p < 0.05$). ICM dosing caused a radical shift in the composition of EPS, as it induced enhanced secretion of high molecular weight and aromatic proteins (tyrosine and tryptophan). ICM also resulted in reduction of the oxygen uptake capacity of the microbial sludge and increment in its floc-size distribution. However, no adverse effects were inflicted on the total organic carbon (TOC) and ammonium removal performance of the MBR, even at high ICM concentration of 5 mg/L. Iohexol and iopromide were found to be moderately degradable in the MBR (average removal efficiencies ranging ~40-50%), whereas iopamidol was found to be highly recalcitrant (average removal of <10%). Further, potential ICM degrading strains- *Zoogloea* and *Bdellovibrio* (which may take part in ICM removal pathway) were identified in this study. The present study is the first study to elucidate the effects of ICM on the fouling propensity of MBR, and identify the potential ICM degrading strains.

The fate of the two ICM (iohexol and iopamidol) was also assessed in a lab-scale PMR. To represent real scenario, degradation of the ICM was studied in tap water and WWTP effluent (from Büsnau WWTP, Germany), and effects of different operational variables of the PMR on the degradation of the ICM were elucidated. The maximum removal of iohexol and iopamidol achieved was ~53 and ~22%, respectively, at 21.4 min residence time, 26 mW/cm² of UVA fluence, and in distilled water matrix. Increasing the UVA intensity and residence time in the PMR was found to positively affect the removal of the ICM. On the other hand, experiments performed in tap water and WWTP effluent indicated severe inhibition in the removal of the two ICM.

Overall, the present study has highlighted the priority PPCPs that need to be put on the watch list for the Indian context. This study can be helpful in setting up regulatory guidelines for the risk causing PPCPs. Further, considering the high RQ values obtained in this study, there is an immediate requirement of upgradation of the existing treatment facilities to reduce the PPCP load in the Indian environmental waters. The findings drawn from the lab experiments suggest that the presence of high amount of ICM in wastewater (such as hospital effluent or waste from radiology wards) can have adverse effects on sludge characteristics and can result in increased running cost of MBR. Further, in this study, assessment of the fate of the ICM in a complete treatment train, including secondary (MBR) and tertiary (PMR) treatment stage of WWTP was done by conducting lab-scale experiments. The findings drawn from this study would be useful for drawing insights on optimizing the process variables of MBR and PMR technology to enhance ICM removal, and reduce their burden in the environmental waters.

सार

पर्यावरणीय जल में फार्मास्यूटिकल्स का स्राव, उनके विखंडित ना होने वाले लक्षणों, अतः जलीय जीवन को नुकसान पहुंचाने के कारण एक जरूरी मुद्दा बन गया है। प्रमुख मार्ग जिसके द्वारा फार्मास्यूटिकल्स पर्यावरण में प्रवेश करते हैं, अपशिष्ट जल उपचार संयंत्र (डब्ल्यू डब्ल्यू टी पी) के प्रवाह निर्वहन के माध्यम से होता है। उच्च स्व-दवा दरों, आंशिक अपशिष्ट जल उपचार कवरेज, और भारत एक फार्मास्यूटिकल निर्माण केंद्र होने के कारण, फार्मास्यूटिकल्स के साथ भारतीय पर्यावरणीय जल का प्रदूषण गंभीर है। भारत के पर्यावरणीय जल में फार्मास्यूटिकल्स के कई घटनाओं के अध्ययन के बावजूद, एक व्यापक जोखिम मूल्यांकन अध्ययन की अभी भी कमी थी। फार्मास्यूटिकल्स के बीच, आयोडीनयुक्त एक्स-रे कंट्रास्ट मीडिया (आई सी एम) फार्मास्यूटिकल्स का एक वर्ग है जो अंग इमेजिंग उद्देश्यों के लिए चिकित्सा परीक्षाओं में उच्च मात्रा में उपयोग किया जाता है। डब्ल्यू डब्ल्यू टी पी ने आई सी एम को विखंडित करने में असमर्थता दिखाई है, और आई सी एम युक्त पानी के कीटाणुनाशन ने अत्यधिक साइटोटॉक्सिक और जीनोटॉक्सिक आयोडीन युक्त कीटाणुशोधन उपोत्पादों का निर्माण दिखाया है। अन्य फार्मास्यूटिकल वर्गों पर कई अध्ययन के बावजूद, आई सी एम पर सीमित शोध कार्य हुए हैं। इन कारणों को ध्यान में रखते हुए, वर्तमान अध्ययन ने विभिन्न पर्यावरणीय जल में फार्मास्यूटिकल्स की उपस्थिति से भारत के पूर्ण जोखिम प्रोफाइल का मूल्यांकन करने पर ध्यान केंद्रित किया है, और एक लैब-स्केल मेम्ब्रेन बायोरिएक्टर (एमबीआर) में एक अड़ियल फार्मास्यूटिकल वर्ग- आई सी एम के प्रपांतरण का अध्ययन किया है। इस अध्ययन को लैब-स्केल फोटोकैटलिटिक मेम्ब्रेन रिएक्टर (पी एम आर) में आई सी एम की विधना का आकलन करने के लिए भी बढ़ाया गया है, इसलिए एक विशिष्ट डब्ल्यू डब्ल्यू टी पी ऑपरेशन के द्वितीयक (एम बी आर) और तृतीयक (पी एम आर) उपचार चरण में उनके पूर्ण भाग्य का चित्रण किया गया।

यह अध्ययन पर्यावरणीय जल में विभिन्न प्रकार के फार्मास्यूटिकल्स की उपस्थिति के कारण मानव स्वास्थ्य, रोगाणुरोधी प्रतिरोध (ए एम आर) चयन, और जलीय जीवन के लिए जोखिम की गणना करता है। अध्ययन ने भारतीय पर्यावरणीय जल में व्यक्तिगत देखभाल उत्पादों (पी सी पी) की उपस्थिति से होने वाले जोखिम का भी विश्लेषण किया ताकि भारतीय जल मैट्रिक्स में उनके प्रदूषण को भी चित्रित किया जा सके। इस अध्ययन के परिणामों ने संकेत दिया कि भारतीय पर्यावरणीय जल में पाए गए फार्मास्यूटिकल्स और पर्सनल केयर प्रोडक्ट्स (पी पी सी पी) (98 में से) लगभग आधे संभावित जोखिम (जोखिम भागफल, $RQ > 1$) का कारण बनते हैं, या तो जलीय प्रजातियों, मानव के स्वास्थ्य, अथवा ए एम आर चयन के लिये।

एमबीआर एक उन्नत जैविक अपशिष्ट जल उपचार तकनीक है, जिसने उच्च स्लज रिटेंशन टाइम (एसआरटी) और मिक्स्ड लिकर सस्पेंडेड सॉलिड्स (एमएलएसएस) होने की अपनी क्षमता के कारण पर्यावरण में फार्मास्यूटिकल्स की रिहाई के खिलाफ बाधा डालने में आशाजनक परिणाम दिखाए हैं। इसलिए, वर्तमान अध्ययन ने एक लैब-स्केल एमबीआर सिस्टम के दीर्घकालिक संचालन में तीन आई सी एम (आईहेक्सोल, आईप्रोमाइड, आईपामेडोल) के भाग्य का अध्ययन किया है, और एम बी आर के प्रदर्शन पर उनके प्रभावों का भी अवलोकन किया है।

इस अध्ययन में पाया गया कि आईसीएम की उपस्थिति एमबीआर में स्लज की विशेषताओं में बदलाव जैसे बाह्य कोशिकीय बहुलक पदार्थों (ईपीएस) ($P < 0.05$) की बढ़ी हुई मात्रा में बदलाव के कारण मेम्ब्रेन दूषण को बढ़ा सकती है। आईसीएम की खुराक ने ईपीएस की संरचना में एक क्रांतिकारी बदलाव का कारण बना, क्योंकि यह उच्च मोलेकुलर वेट और ऐरोमेटिक प्रोटीन (टायरोसिन और ट्रिप्टोफैन) के बढ़े हुए साव को प्रेरित करता है। आई सी एम के परिणामस्वरूप माइक्रोबियल स्लज की ऑक्सीजन ग्रहण क्षमता में कमी आई और इसके फ्लोक-साइज़ वितरण में वृद्धि हुई। हालांकि, एमबीआर के कुल जैविक कार्बन (टीओसी) और अमोनियम हटाने के प्रदर्शन पर कोई प्रतिकूल प्रभाव नहीं पड़ा, यहां तक कि 5 मिलीग्राम / लीटर की उच्च आईसीएम मात्रा पर भी। एमबीआर ने आईहेक्सोल और आईप्रोमाइड को

औसतन ~ 40-50% हटाने की क्षमता योग्य पाया गया, जबकि आईपामेडोल को औसतन <10% हटाया। इसके अलावा, इस अध्ययन में संभावित आईसीएम डिग्रेडिंग स्ट्रेन- जूग्लोइया (*Zoogloea*) और बिदेलोविव्रियो (*Bdellovibrio*) (जो आईसीएम रिमूवल पाथवे में भाग ले सकते हैं) की पहचान की गई। वर्तमान अध्ययन एमबीआर की मेम्ब्रेन दूषण प्रवृत्ति पर आईसीएम के प्रभावों को स्पष्ट करने और संभावित आईसीएम अपमानजनक उपभेदों की पहचान करने वाला पहला अध्ययन है।

लैब-स्केल पीएमआर में दो आईसीएम (आईहेक्सोल और आईपामेडोल) के भाग्य का भी आकलन किया गया है। वास्तविक परिदृश्य का प्रतिनिधित्व करने के लिए, आईसीएम के क्षरण का अध्ययन नल के पानी और डब्ल्यू डब्ल्यू टी पी के बहिःस्राव (बुसनौ डब्ल्यू डब्ल्यू टी पी, जर्मनी से) में किया गया है, और आईसीएम के क्षरण पर पी एम आर के विभिन्न परिचालन चर के प्रभावों को स्पष्ट किया गया है। आईहेक्सोल और आईपामेडोल का अधिकतम निष्कासन क्रमशः ~53 और ~22% था, 21.4 मिनट के निवास समय पर, 26 mW/cm² UVA प्रवाह और आसुत जल मैट्रिक्स में। पीएमआर में यूवीए तीव्रता और निवास समय में वृद्धि आईसीएम को हटाने को सकारात्मक रूप से प्रभावित करने के लिए पाया गया। दूसरी ओर, नल के पानी और डब्ल्यूडब्ल्यूटीपी के बहिःस्राव में किए गए प्रयोगों ने दो आईसीएम को हटाने में गंभीर अवरोध का संकेत दिया।

कुल मिलाकर, वर्तमान अध्ययन ने उन प्राथमिकता वाले पीपीसीपी पर प्रकाश डाला है जिन्हें भारतीय संदर्भ के लिए निगरानी सूची में रखने की आवश्यकता है। यह अध्ययन पीपीसीपी के कारण होने वाले जोखिम के लिए नियामक दिशानिर्देश स्थापित करने में सहायक हो सकता है। इसके अलावा, इस अध्ययन में प्राप्त उच्च आरक्यू मूल्यों पर विचार करते हुए, भारतीय पर्यावरणीय जल में पीपीसीपी भार को कम करने के लिए मौजूदा उपचार सुविधाओं के उन्नयन की तत्काल आवश्यकता है। प्रयोगशाला प्रयोगों से निकाले गए निष्कर्षों से पता चलता है कि अपशिष्ट जल में आईसीएम की उच्च मात्रा की उपस्थिति (जैसे कि अस्पताल के अपशिष्ट या रेडियोलॉजी वार्ड से अपशिष्ट) स्लज की विशेषताओं पर

प्रतिकूल प्रभाव डाल सकती है और इसके परिणामस्वरूप एमबीआर की लागत में वृद्धि हो सकती है। इसके अलावा, इस अध्ययन में, डब्ल्यूडब्ल्यूटीपी के माध्यमिक (एमबीआर) और तृतीयक (पीएमआर) उपचार चरण सहित एक पूर्ण उपचार श्रृंखला में आईसीएम के भाग्य का मूल्यांकन प्रयोगशाला-स्तरीय प्रयोगों का संचालन करके किया गया है। इस अध्ययन से निकाले गए निष्कर्ष आईसीएम हटाने को और पर्यावरणीय जल में उनके बोझ को कम करने के लिए एमबीआर और पीएमआर प्रौद्योगिकी के प्रक्रिया चर के अनुकूलन पर अंतर्दृष्टि प्राप्त करने के लिए उपयोगी होंगे।

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NOMENCLATURE

WWTP	Wastewater treatment plant
AMR	Antimicrobial resistance
RQ	Risk quotient
PCPs	Personal care products
ECs	Emerging contaminants
MBR	Membrane bioreactor
CAS	Conventional activated sludge
SRT	Solids retention time
EPS	Extra cellular polymeric substance
SMP	Soluble microbial product
ICM	Iodinated X-ray contrast media
PMR	Photocatalytic membrane reactor
WTP	Water treatment plant
DWEL	Drinking water equivalent level
PNEC	Predicted no effect concentration value
MIC	Minimum inhibition concentration
CW	Constructed wetland
IFAS	Integrated fixed film activated sludge
MLSS	Mixed liquor suspended solids
AOB	Ammonium oxidizing bacteria
COD	Chemical oxygen demand
TMP	Trans membrane pressure
MW	Molecular weight
MWCO	Molecular weight cut off
AMO	Ammonium monooxygenase
OLR	Organic loading rate
NLR	Nitrogen loading rate
BW	Body weight
K_{biol}	Pseudo-first order biodegradation rate coefficient
K_d	Solid-water distribution coefficient

SNR	Specific nitrification rate
SNA	Specific nitrifying activity
UV-LEDs	Ultraviolet light emitting diodes
ADI	Acceptable daily intake
PPCPs	Pharmaceuticals and personal care products
MEC	Maximum measured environmental concentration values
ChVs	Chronic toxicity values
POD	Point of departure
NOAEL	No-observed adverse effect level
LTD	Lowest therapeutic dose
AF	Assessment factor
SF	Safety factor
LOAEL	Low observed adverse effect level
EUCAST	European committee on antimicrobial susceptibility testing
ECOSAR	Ecological structure activity relationship
QSAR	Quantitative structure activity relationship
TGD	Technical guidance document
CETP	Common effluent treatment plant
WHO	World health organization
STP	Sewage treatment plant
PBT	Persistence bioaccumulation toxicity index
PEC	Predicted environmental concentration
HQ	Hazard Quotient
SEC	Size exclusion chromatography
EEM	Excitation emission matrix
BSA	Bovine serum albumin
PES	Polyethersulfone
DO	Dissolved oxygen
HRT	Hydraulic retention time
RI	Refractive index
ACN	Acetonitrile
DI	Deionized water
TOC	Total organic carbon

SOUR	Specific oxygen uptake rate
OTU	Operational taxonomic unit
SEM	Scanning electron microscope
EDX	Energy dispersive X-ray
AFM	Atomic force microscopy
FT-IR	Fourier transform infrared spectroscopy
P/C	Protein/carbohydrate ratio
FRI	Fluorescence regional integration
F/M	Food to mass ratio
RMS	Root mean square
HPLC	High performance liquid chromatography
PDA	Photo diode array detector
RSD	Relative standard deviation
LOD	Limit of detection
LOQ	Limit of quantification
A2O	Anaerobic-anoxic-oxic
MBBR	Moving bed biofilm reactor
EPD	Electrophoretic deposition method
TW	Tap water
WW	Wastewater treatment plant effluent
DAD	Diode array detector
TPs	Transformation products
MSC	Minimal selective concentration