Chapter 2
Literature Review

2.1 Common Types of Emerging Pollutants (EPs) in Rivers

Emerging pollutants are new compounds detected in low concentrations in surface and groundwater that have been released into the environment for a long time. The synthesis of new chemicals or changes in the use and disposal of existing chemicals create new sources for emerging pollutants (http://www.norman-network.net). According to the definition given by the United States Geological Survey, EPs are all synthetic or naturally occurring chemicals that are not included in the routine monitoring program but have the potential to enter the environment and cause known or suspected adverse ecological, (eco) toxicity, and/or human health effects (USGS, 2017). The detection of EPs in many rivers worldwide has created a cause of concern and an environmental challenge in recent years (Bolong et al., 2009; Geissen et al., 2015; Maria Gavrilescu et al., 2015; Philip et al., 2018). However, these pollutants have yet to be monitored routinely due to their low concentrations and acceptable detection methods. They are now being examined seriously as they have been found to influence the ecological function of rivers and water bodies (Farre et al., 2008; Poynton and Robinson, 2018).

Based on sources and differing physiochemical characteristics, EPs are broadly categorized into six major classes based on presence in river waters: (i) Personal Care Products (PCPs), (ii) Endocrine-Disrupting Chemicals (EDCs), (iii) Pharmaceutical Pollutants (PPs), (iv) Persistent Organic Pollutants (POPs), (v) Artificial Sweeteners (ASs), and (vi) Microplastics (MPs) (http://www.norman-network.net). The presence of these compounds in the river environment at high concentrations beyond certain limits is a cause of concern and needs to be studied in greater detail.

2.1.1 Personal Care Products (PCPs)

The presence of personal care products (PCPs) in river water is an emerging environmental concern. PCPs comprise a large and diverse group of organic compounds like hydroxyl (-OH), carboxyl (-COOH), and amine (-NH2) groups and their products include a variety of chemicals used in items like shampoos, soaps, cosmetics, sunscreens, and deodorants. When these products are washed off, they enter wastewater systems and, in many cases, find their way into natural water bodies, including rivers. Triclosan, N, N-diethyl-meta-toluamide, and Salicylic acid are the compounds reported in rivers mainly used as antimicrobials, insect repellents, and skin disorders.

Consumption of PCPs in large quantities, often in higher doses and frequencies than recommended (Daughton and Ternes., 1999; Mandaric et al., 2017) is the cause of concern. PCPs such as polycyclic aromatic hydrocarbons were reported in river Gomti, having a concentration of 10.33 μg/L (Singh Kunwar et al., 2006).

2.1.2 Endocrine-disrupting compounds (EDCs)

EDCs, defined by the U.S. Environmental Protection Agency (EPA), are ‘exogenous agents that disrupt synthesis, secretion, transport, metabolism, and binding effects in living organisms. EDCs eliminate natural blood hormones in the body and are responsible for homeostasis, fertility, reproduction, and development. It also causes severe neurological and immune system damage. The effects of EDCs are toxic in very low concentrations, although the exact limiting values have not been established because the toxicity potential depends on the respective organism. (Vilela et al., 2018). Bisphenol-A, Perfluoroalkyl substances (perfluorooctanoic acid and perfluorooctanoic sulfonate) and Pesticides (Atrazine and 2,4- Dichlorophenoxyacetic acid) are the chemicals of concern majorly reported in river waters (Sharma et al., 2016).

2.1.3 Pharmaceutical Pollutants (PPs)

PPs are those substances used by an individual for personal health care and agribusiness products to promote farm animals' health or growth. It includes prescription drugs, nonprescription drugs, and veterinary drugs. Four PPs classes, such as antibiotics, non-steroid anti-inflammatory drugs (NSAIDs), anticonvulsants, and stimulants, are reported in river waters. In a report by Bhagat et al. (2018), antibiotics account for 67.3% of prescription drugs, including ceftriaxone (69%), followed by amoxicillin (61%), ciprofloxacin (16%), and ofloxacin (7%). The occurrence of these pollutants in river waters with concentrations from ng/L to µg/L and their effects on the microbiological consortium have been reported (Sharma et al., 2019; Mutiyar et al., 2018; Subedi et al., 2018; Williams et al., 2019; Kumar et al., 2019; Fick et al., 2009; Mutiyar et al., 2014a, 2014b & 2018).

2.1.4 Persistent Organic Pollutants (POPs)

POPs are anthropogenic chemicals that withstand most environmental degradation processes and accumulate in living organisms with a slow metabolism. Chemicals are organic in nature and are persistent, non-volatile, and lipophilic properties; they mix with particles in the air (snow, fog, and rain) and are transported over long distances from their source into the atmosphere (Islam et al., 2018 Han and Currell, 2017). The presence of POPs has been reported in places where these pollutants have never been used, e.g., poles of the earth (Jolly Jacob and Jacob Cherian 2013). The ability to bio-magnify, bioaccumulate, and long-range environmental transport properties transform in the food chain (animal and human) with slow metabolism that makes POPs toxic and seriously threatens human health and nature (Sharma et al., 2014). Use of pesticides and herbicides from agriculture, chemicals released after burning of plastics, and chemicals released POPs into the environment. Dichlorodiphenyltrichloroethane (DDT), Hexachlorobenzene

(HCB), dioxins, and furans are the common POPs reported in river water (Rajan et al., 2023; Ashesh et al., 2022).

2.1.5 Artificial Sweeteners (ASs)

ASs is used as sugar substitutes in foods and beverages because they have a longer shelf life, are low in calories, and are chemically stable (Praveena et al., 2019). Mainly four types of AS have higher consumption levels, namely aspartame (soft drinks, beverages, tabletop sweeteners, cereals, tea beverages, sugar-free chewing gums), acesulfame K2 (carbonated beverages), saccharin (a variety of beverages, foods, cosmetics, and pharmaceuticals) and sucralose (baking or in products that require a longer shelf life) (FSSAI, Indian regulator). The world consumption of non-nutritious artificial sweeteners has been estimated at more than 159,000 tons, with a market value of 2 billion US dollars (Euromonitor International, 2017). It used to be considered safe at an acceptable daily dose. In India, the Prevention of Adulteration of Food Act allowed the addition of 100 mg/kg saccharin (SAC) to carbonated beverages. In addition, some products, such as pan masala and crushed ice, have been reported to contain up to 24.30 gm SAC/kg (Tripathi et al., 2006). Acesulfame and Sucralose are particularly suitable for diabetics and are cited as the most sustainable sweeteners, with removal rates of only 40% and 20%, respectively (Scheurer et al., 2009; Zygler et al., 2009). ASs such as saccharine (85 ng/L), sucralose (24 ng/L), and cyclamate (1.2 ng/L) are present in river Ganga (Sharma et al., 2019). Persistent aquatic toxicity and ecosystem disruption are the properties of major concern affecting the river environment. Conventional sewage treatment plants have limited ability to remove these artificial sweeteners. Treated wastewater from sewage treatment plants is an important point source of artificial sweeteners in the aquatic environment (Praveena et al., 2019).

2.1.6 Microplastic (MPs)

MPs are an increasingly growing pollutant with a particle size between 1 mm and 5 mm. According to Lebreton (2017), 1.15- 2.41 million tons of plastic are transported through rivers into the sea every year. Degradation, fragmentation, and leaching of additives change the density of plastic objects and lead to the formation of microplastics. Near the Rameshwaram coast, India, 403-423 pieces of polyethylene MPs have been reported in water. The fate of MPs depends primarily on polymer density, which affects their position in nature and the blocking of drainage systems, including uptake by animal entanglement and aesthetic effects (Avio et al., 2017; Ryan et al., 2009). Processes such as biofouling and the settlement of organisms on the plastic surface increase the weight of the particles, which increases the possibility of interaction with biota and thus accelerates their sinking to the ground (Lobelle & Cunliffe 2011).

Among six EPs reported in rivers, pharmaceuticals act as pseudo-persistent pollutants (Ellis, 2006) and, as such, can have undesirable and unexpected effects on living organisms and the environment (Liu & Wong 2013). The major concern reported by researchers worldwide is due to the high and frequently reported presence of pharmaceuticals above their PNEC value in river water. Measured environmental concentration (MEC) above the PNEC affects biotic life survival because of the persistent nature, bioaccumulation, biomagnification, and toxicity to different trophic-level aquatic organisms (Ebele et al., 2017) PPs have been taken as causative water quality parameters for river health index assessment.

2.2 Common Types of Pharmaceutical Pollutants (PPs) in Rivers

India has the second-largest share of the pharmaceutical sector, followed by China, with a maximum annual turnover accounting for 71% of the global market. The current market for the pharmaceutical industry is $42 billion, and it may reach as much as $120-

130 billion by 2030 due to innovative technology, quality research, and cheap production (IBEF, 2021). India is also the world's largest supplier of generic medicines, accounting for 20% of global exports by volume. Among different pharmaceutical classes, antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, and stimulants inhibit the spread of infectious organisms. This group of PPs constitutes around 13.6 % of total production. Antibiotic drug consumption is much higher in India than in other countries all around the world. Regarding concentrations and frequency of occurrence, antibiotics are the highest, followed by the residue of NSAIDs, anticonvulsants, and stimulants.

2.2.1 Antibiotics

India and China are the world-leading countries in antibiotic production. It accounts for 80 to 90% of global antibiotic production. Antibiotics treat and prevent bacterial infections in humans and animals (Nathan, 2014). It also grows aquaculture farms and animal husbandry (Van Boeckel et al., 2017). Different representative chemicals of the antibiotics class include norfloxacin, ofloxacin, ciprofloxacin, chloramphenicol, azithromycin, amoxicillin, ampicillin, sparfloxacin, naproxen, trimethoprim, etc. Antibiotic residues may bioaccumulate in the human body through excess consumption of medication. Studies conducted in Shanghai showed the presence of more than 20 antibiotics in urine samples from children (Xu et al., 2016). The source of 90% of the antibiotics reported in wastewater is excreted unchanged in the urine and/or feces (Hirsch et al., 1998; Pan et al., 2011; Hu et al., 2010). The highest observed concentration of ampicillin in human feces is 49.52 μg kg^{-1}, and in urine, it shows a concentration of more than 40 μgL^{-1} (Ji et al., 2010; Xu et al., 2015). Continuous exposure to antibiotics in the human body intensifies the effects of antibiotic-resistant pathogenic strains (Zhan et al., 2018). An increase in antibiotic-resistant bacteria (ABRB) is a cause for concern. Antibiotic resistance is the ability of bacteria to resist and escape the effect of antibacterial drugs that were once effective in treating the

bacteria. Consequently, a high dose of medication is required to cure a disease due to an increase in the resistivity of drugs on the microbial consortium. Almost 7 lakh people worldwide lose their lives to resistant infections each year (IDMA, 2018). The World Health Organization (WHO) has endorsed a global action plan to combat ABRB, including the major drug resistance trend. The Government of India has also approved the National Plan of Action to Combat Antibiotic Resistance (Department of Health and Family Welfare, 2017).

In India, the Isakavagu-Nakkavagu stream near Hyderabad, which eventually drains into the river Godavari, has been reported to have the highest concentration of antibiotics (ciprofloxacin- 250 µg/L and norfloxacin- 470 µg/L) (Fick et al., 2009). The area near pharmaceutical manufacturing facilities and hospital-prone locations are the major point sources of pharmaceutical contamination of water bodies, especially when wastewater treatment units are technologically inefficient in removing pollutants.

2.2.2 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs are widely consumed around the world and have properties to treat muscle pain, fever, and joint inflammation in humans and animals (Parolini et al., 2020). It includes analgesic (for relieving pains) and anti-inflammatory (reducing redness, swelling, and pains) classes of pharmaceutical products. NSAIDs are used as both prescription and nonprescription drugs because of their disease-curing properties. Different representative chemicals of analgesic and anti-inflammatory classes include ibuprofen, ketoprofen, acetaminophen, and diclofenac, which are majorly reported in rivers worldwide. Among analgesics, acetaminophen is India's most widely used nonprescription drug (to treat mild to moderate pain from headaches, toothaches, backaches, or cold/flu and to reduce fever) (Soumya et al., 2016). In natural water systems, the maximum concentration reported in India is for ibuprofen (2.32 µg/L in the Cooun river near Chennai followed by

acetaminophen (1.56 µg/L) and ketoprofen (1.07 µg/L) in the river Ganga near Sahibganj, Bihar (Subedi et al., 2015). Due to the presence of these pollutants in river water, a moderate to high ecological risk has been reported (Mutiyar et al., 2018; Sharma et al., 2019).

2.2.3 Anticonvulsants

Anticonvulsants, in particular, are prescribed to prevent migraines, rapid cycles of mania, and depression (JCY et. al., 2014). Chemical compounds are used to calm brain hyperactivity as a mood stabilizer in patients with bipolar disorder, neurogenic diabetes, and alcohol withdrawal. Carbamazepine, phenytoin, gabapentin, and lamotrigine etc. are the anticonvulsant that is found in various rivers. The highest concentration of carbamazepine (1.346 µg/L) is reported in river Yamuna (near Agra) followed by 0.570 µg/L in river Ahar (Udaipur) and 0.008 µg/L in river Brahmaputra (Williams et al., 2019; Mutiyar et al., 2018). Carbamazepine has a high risk for aquatic organisms, mainly fish, even at low availability in surface water (Zhou et al., 2019). Effluent from the STPs in southern states of India reported high release of carbamazepine ranging between 4.78-57.6 mg/d/1000 people (Subedi et al., 2015).

2.2.4 Stimulant

Stimulants are psychoactive chemicals that encourage rational and physical activity. It contains organic nitrogen compounds that are present in the form of alkaloids. Amine, hydroxyl, and methyl group compounds with lipophilic properties are the main characteristics of stimulants. Caffeine, amphetamine, and methamphetamine are some compounds found in river waters. The consumption of caffeine and amphetamines is very frequent worldwide due to their ability to increase work efficiency and mental concentration (Yotam et al., 2014). In India, the beverage is one of the main sources of stimulant compounds in water. The caffeine content in non-alcoholic beverages with more

than 145 mg/L is labeled as caffeinated (FSSAI 2016). Baselt et al. (2020) observed that about 30-62% of the stimulants are released in the urine within 24 hours of ingestion. Amphetamine and caffeine are essential stimulants commonly found in high concentrations in surface water. In Cooun River, Chennai, India, amphetamine (0.984 µg /L) has been reported. A caffeine concentration of 0.11 µg/L (Mutiyar et al., 2018) was found in the river Yamuna (near Agra), 3.68 µg/L (Williams et al., 2019) in the river Ahar near Udaipur, and 7.43 µg/L in the river Ganga (Sharma et al., 2019).

2.3 Sources of Pharmaceutical Pollutants (PPs) in Rivers

PPs enter the rivers through discharge from two types of sources (Bolong et al., 2009, Geissen et al., 2015):

2.3.1 Point Sources

Medicine manufacturing industries, sewage treatment plants (STPs) and hospital wastewater are the major point sources for the presence of pharmaceuticals in river waters. Worldwide, the concentrations of PPs reaching STPs range from ng/L to µg/L (Coetiser et al., 2009; Nadia et al., 2022; Vaudreuil et al., 2024). As conventional technology based STPs do not remove PPs to significant levels, STPs may form a point source of discharge of PPs to rivers.

2.3.2 Non-point Sources

Runoff carrying effluents of septic tanks spread across an area and release of untreated or partially treated wastewater from residential units discharging into water courses contribute PPs in river waters (Larsson et al., 2007). Hospital wastewater streams from diagnostic services (laboratories, transfusion centers, radiology departments) and general wards (medicine and surgical unit are another source, which once mixed with domestic wastewater and discharged to rivers increase the pharmaceutical load.

Unregulated discharges of leachates from municipal solid wastes also increase the load of pharmaceutical pollutants, especially during the first flush of rain events (Ramakrishnan et al., 2015). Wu et al. (2015) reported high concentrations of 20 antibiotics in seepage water samples from two transfer stations of municipal solid waste from China, which contained unwanted/ obsolete household drugs.

Human urine and feces carry high concentrations of PPs as up to 80-90 % of pharmaceutical compounds consumed by a person usually get excreted as the metabolites of the same pharmaceutical compounds (Buerge et al., 2003), eventually reaching the septic tanks and from there to other water bodies through seepage, effluents, or overflows. Caffeine, a frequently reported PP in rivers worldwide, is mainly found in cough syrup, energy drinks, and processed food. Adults often consume it as a mood-altering drug that finally reaches domestic wastewater through urine discharge. A schematic flow diagram for PPs from the originating source to the water environment is detailed in Fig. 2.1

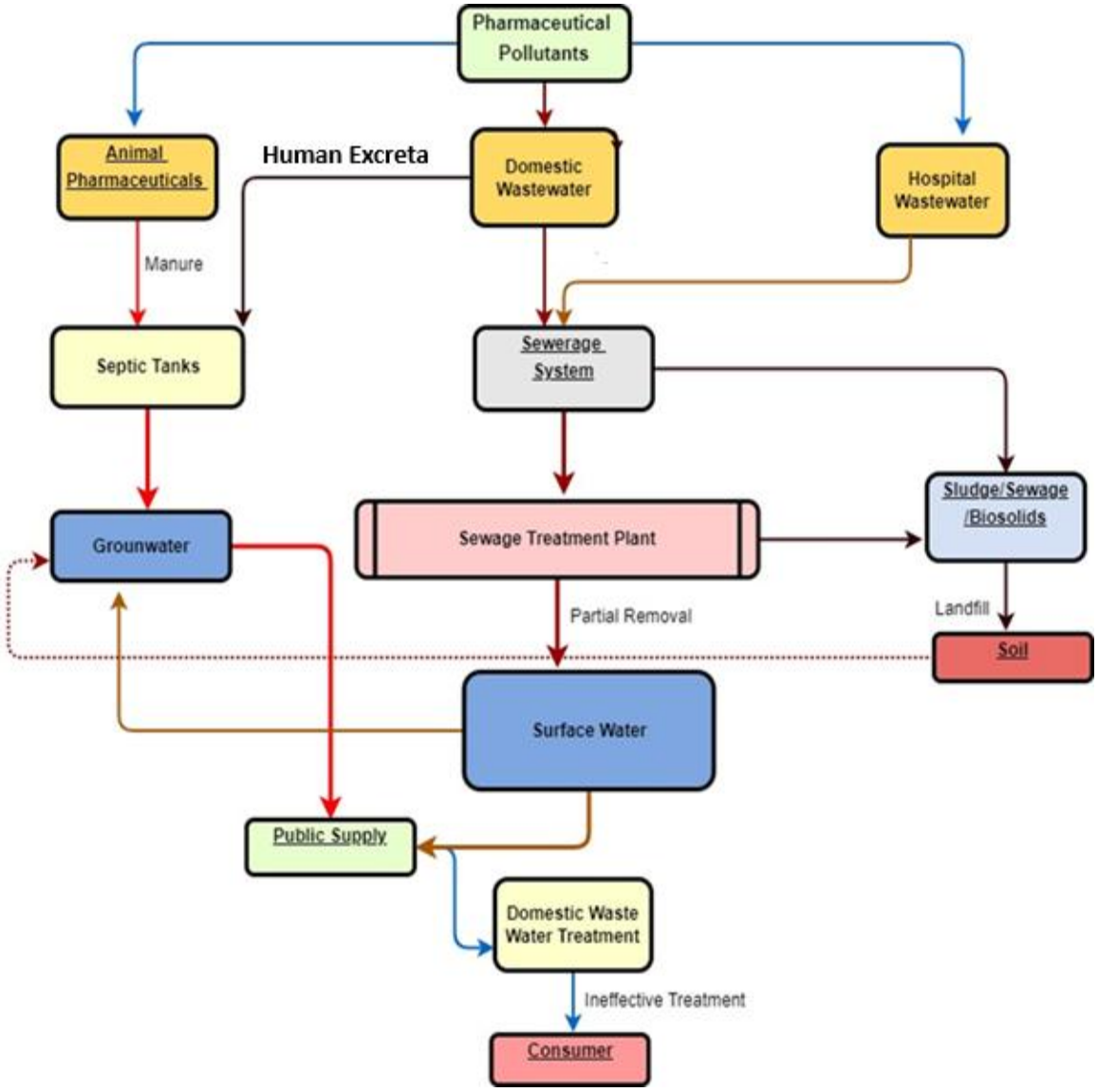


Fig. 2.1: Schematic flow diagram for PPs from originating source to the water environment.

2.4 Some Physicochemical Characteristics of Pharmaceutical Pollutants (PPs)

The physicochemical characteristics such as partition coefficient (log K_{ow}) and ionization constant (pKa) help determine the persistent nature of organic pollutants and the ability to donate protons of a chemical, respectively.

2.4.1 Partition Coefficient (log K_{ow})

For compounds with molecular weight <1000 that are small enough to be absorbed through membranes, log K_{ow} can characterize a compound's affinity for cell membranes and, thereby, its tendency to bioaccumulate (Sanderson et al. 2004).

log K_{ow} represents the distribution of a substance in different environmental compartments (water, soil, air, aquatic biota, etc.). High log K_{ow} values tend to absorb more organic matter as their low affinity for water also has the potential for bioconcentration in living organisms. Pollutants with a log K_{ow} value of more than 3.0 show hydrophobic behaviour, leading to a high potential for bioaccumulating these chemicals (Palma et al., 2014). For example, ibuprofen, ketoprofen, azithromycin, and naproxen can persist in the environment for a long time and have high bioaccumulation properties.

2.4.2 Ionization Constant (pKa)

The ionization constant (pKa) is a crucial property of pharmaceutical compounds because it influences their solubility, permeability, stability, absorption, distribution, metabolism, excretion, and toxicity. Understanding the pKa of a drug helps predict its behavior in different physiological environments.

pKa denotes the acid dissociation constant in an aqueous solution. It represents the strength of the acid and the ability to donate its protons. A lower pKa value indicates a stronger acid and a greater ability to donate its protons. Ampicillin with a pKa = 3.2 represents the strong acid, while carbamazepine with pKa= 13.9 represents a weak acid.

Such properties of some common pharmaceutical classes of compounds have been given in Table 2.1.

Table 2.1: Common pharmaceutical chemicals and their physicochemical properties

Pharmaceuticals Class	Representatives Chemicals	Chemical Representations	Mol. wt. (g/mol)	pKa	log K_{ow}	References
1. Antibiotics	Norfloxacin	$C_{16}H_{18}FN_3O_3$	361.37	6.34	0.46	Fick et al.,2009
	Ofloxacin	$C_{18}H_{20}FN_3O_4$	331.34	5.97	-0.39	Mutiyar et al., 2013
	Ciprofloxacin	$C_{17}H_{10}FN_3O_3$	748.99	6.09	0.28	Williams et al.,
	Chloramphenicol	$C_{11}H_{12}Cl_2N_2O_{15}$	323.13	5.5	-1.14	2019
	Azithromycin	$C_{38}H_{76}N_2O_{14}$	785	8.74	4.02	Mutiyar et al., 2014
	Amoxicillin	$C_{38}H_{72}N_2O_{12}$	365.40	3.2	0.87	Choi et. al., 2008.

	Ampicillin	$C_{16}H_{19}N_3O_5S$	349.40	2.5	1.35	
	Sparfloxacin	$C_{19}H_{22}F_2N_4O_3$	392.41	6.25	0.98	
	Naproxen	$C_{14}H_{14}NaO_3$	252.24	4.19	3.18	
	Trimethoprim	$C_{14}H_{18}N_4O_3$	290.32	7.12	0.91	
	Sulfamethoxazole	$C_{10}H_{11}N_3O_3S$	253.28	5.7	0.89	
	Cefuroxime	$C_{16}H_{16}N_4O_8S$	424.38	3.15	-0.16	
	Gatifloxacin	$C_{19}H_{22}FN_3O_4$	375.4	5.94	-0.83	
2.Non-Steroidal Anti-Inflammatory Drugs	Ibuprofen	$C_{13}H_{18}O_2$	206.28	4.91	3.79	Sharma et al., 2019
	Ketoprofen	$C_{16}H_{14}O_3$	254.28	4.45	3.12	Williams et al., 2019
	Acetaminophen	$C_8H_9NO_2$	151.16	9.9	0.46	Mutiyar et al., 2018
	Diclofenac	$C_{14}H_{11}Cl_{12}NO_2$				Subedi et al., 2015.
3.Anticonvulsants	Carbamazepine	$C_{15}H_{12}N_{20}$	236.27	13.9	2.45	Kumar et al., 2019 Mutiyar et al., 2018
4.Stimulant	Caffeine	$C_8H_{10}N_4O_2$	194.19	10.4	-0.07	Sharma et al., 2019
	Amphetamine	$C_9H_{13}N$	135.21	9.9	2.07	Kumar et al.,2019 Williams et al., 2019.

2.5 Methods of Ecological Risk Assessment

Ecological risks due to the toxicity of pharmaceutical compounds are assessed based on Measured Environmental Concentration (MEC) in the river water and Predicted No Effect Concentration (PNEC) for the aquatic organisms of concern. Risk Quotient (RQ), Hazard Quotient (HQ), and Optimized Risk Quotient (RQ_f) are standard methods to estimate the level of risk on biotic groups of organisms present in the aquatic environment (Hernando et al., 2006; Souza et al., 2009; Mutiyar et al., 2014; Sharma et al., 2019; Zhou et al., 2019).

2.5.1 Risk Quotient (RQ)

The risk quotient is calculated using the maximum MEC and the PNEC of the PPs, according to Eq. 2.1 given below (Sharma et al., 2019; Zhou et al., 2019):

$$RQ = \frac{MEC}{PNEC} \quad \text{(Eq. 2.1)}$$

Based on the calculated RQ, the associated risk is classified into three categories (Souza et al., 2009; Hernando et al., 2006):

RQ <0.1, indicates less hazardous effects and thus 'low risk' to the aquatic environment,

0.1<RQ <1, considered as 'moderate risk', and

RQ≥1 is considered to pose a 'high risk' to aquatic organisms.

For the purpose of the present study, some of the PPs whose presence has been reported in river waters and their respective PNEC values for three trophic levels, e.g., Algae, MI, and Fish, have been recorded as given in Table 2.2. The sources of such information include the USEPA ecological structure-activity relationship (ECOSAR v2.0) and several others, as mentioned.

2.5.2 Hazard Quotient (HQ)

Mutiyar et al. (2014) assessed the ecological risks for aquatic organisms based on hazard quotient (HQ). The hazard quotient is the ratio of predicted environmental concentration (PEC) and PNEC. According to Greenhalgh (1987), PEC calculation is difficult in India due to the high rate of medications consumed over the counter without prescriptions. This leads to PEC values that differ from real environmental concentrations. In such cases, the value of measured environmental concentrations (MEC) is taken as the value of PEC. Thus, the HQ may be the same as RQ, which is the ratio of MEC and PNEC (Mutiyar et. al., 2014). Based on estimated HQ, risk management has been classified as RQ from low risk to high risk up to HQ=1.

2.5.3 Optimized Risk Quotient (RQ_f)

The pharmaceutical pollutants are persistent and show their long-term presence in water bodies, thus posing a higher risk to target organisms than pollutants of a non-persistent nature (Desbiolles et al., 2018; Tousova et al., 2017). The optimized risk quotient

(RQ_f) (Zhou, et al., 2019) calculates the risk to aquatic organisms by pollutants after long-term exposure. The calculation is based on the mean RQ value and the frequency of MECs that exceed PNEC. Variation of the concentration of PPs in river water above PNECs is used to screen the pollutants. The RQ_f includes all possibilities for recognizing worst-case scenarios compared to the RQ. RQ_f also encompasses the broad classification of pollutants (high, moderate, tolerable, negligible, and safe) that pose potential risks to aquatic organisms (Zhou, et al., 2019). The RQ_f is calculated using Eq. 2.2 as given below (Zhou, et al., 2019):

$$RQ_f = RQ \times F = \frac{MEC}{PNEC} \times F$$

$$F = \frac{NO1}{NO2} \qquad \text{(Eq. 2.2)}$$

Where F is the Frequency of measured environmental concentrations exceeding PNECs. It is expressed as the ratio of samples with concentrations higher than PNEC (NO_1) and the total number of samples (NO_2). Based on RQ_f estimation, risk measurement is classified into 5 groups (Zhou, et al., 2019):

i. $RQ_f = 0$: no risk is expected at present (safe).
ii. $RQ_f > 0$, but < 0.01: the effect is quite limited (negligible);
iii. $RQ_f \geq 0.01$, but < 0.10: small-scale adverse effect is expected (endurable);
iv. $RQ_f \geq 0.10$, but < 1: Moderate environmental risk is expected (moderate);
v. $RQ_f \geq 1$: High environmental risk is expected (high).

Table 2.2: Common pharmaceutical compounds and their PNEC values for aquatic organisms

S.N.	PPs	PNEC (μg/L) for aquatic organisms			Reference
		Algae	MI	Fish	
i.	Acetaminophen[*2]	13	9.2	38	Calleja et. al., 1994
ii.	Amoxicillin[*1]	5	182.7	--	Holten- Lutzhott et. al., 1999 Eguchi et. al., 2004
iii.	Amphetamine[*4]	3.803	4.357	37.602	ECOSAR
iv.	Ampicillin[*1]	1000	2300	1000	Park & Choi 2008; Kim et al., 2007
v.	Azithromycin[*1]	0.18	0.44	460	Tell et al., 2019
vi.	Caffeine[*4]	0.15	182	87.5	Calleja et. al., 1994
vii.	Carbamazepine[*3]	33.6	13.8	35.4	Kim et al., 2007; Ferrari et al., 2004; Duan et al., 2008
viii	Chloramphenicol[*1]	1259	1000	1900	Zhou et al., 2019; ECOSAR
ix.	Ciprofloxacin[*1]	2790	8049	1705	ECOSAR
x.	Diclofenac[*2]	0.2	20	0.050	Lawrence et. al., 2007/ Haap et. al., 2008/ Hoeger et. al., 2005
xi.	Ibuprofen[*2]	4	9.1	170	KNOL/BASF 1995
xii.	Ketoprofen[*2]	160	250	32	Sanderson et al., 2003
xiii	Naproxen[*1]	31.80	2.620	115.2	Isidori et. al., 2005; Quinn B. et. al., 2008; Li Q. et al., 2016
xiv.	Norfloxacin[*1]	1.6	12	1.4	Ando et al., 2007/ECOSAR
xv.	Ofloxacin[*1]	5	31.75	101	Isidori et al., 2005; USEPA (2012)
xvi.	Sulfamethoxazole[*1]:	0.27	25	506	Ferrari et al., 2004/Kim et. al., 2007/Garcia- Galan et. al., 2012
xvi	Trimethoprim[*1]	795	120.7	16	Kim et al., 2007; Grung et al., 2008; Sanderson et al., 2003

2.6 Toxic Effects of the Pharmaceutical Compounds on Aquatic Organisms

The reported toxic effects of fifteen pharmaceutical compounds reported above the PNEC in river waters on Algae, MI, and Fish have been summarized in Table 2.3.

Table 2.3: Pharmaceutical compounds and their toxic effects on aquatic organisms

S.N.	Pharmaceutical Compounds	Toxicity effects on aquatic organisms		
		Algae	Macroinvertebrates	Fish
i.	Ampicillin	• Increases mortality in Vibrio fischeri group of bacteria (Mutiyar and Mittal 2014).	------	• Increases mortality, show agitated swimming, air gulping, loss of equilibrium, and hemorrhage within the 96-hours exposure (Sogbesan et al., 2017).
ii.	Azithromycin	------	• Decrease in digestive enzymes to macroinvertebrates (Daphnia Magna) (Li et al., 2020).	• Exposure of azithromycin to zebrafish (Danio rerio) causes cardiotoxicity, which increases heart rate and fluid around the heart. (Yan et al., 2019).
iii.	Acetaminophen	------	• Affects growth and causes 50 % mortality rate to daphnia magna after 21 days at exposure of concentration 2-4 mg/L (Du et al., 2016).	• It alters the swimming behaviour of fish at 100 µg/L and affects embryo abnormalities in zebrafish at a concentration higher than 2500 µg/L (David et al., 2009; Escapa et al., 2019).
iv.	Amoxicillin	• Growth inhibition and affect photosynthesis via inhibiting chloroplast formation and protein biosynthesis (Liu et al., 2016; Liu et al., 2018).	• Population growth rate decreases in daphnia magna at 21-d chronic toxicity test (Lee et al., 2021).	• Exposure for 96h leads to oxidative stress and hatching of embryos at a dose of 135-170 mg/L (Oliveira et al., 2013).
v.	Caffeine	• Causes protein sensitivity due to polypeptides in algae species. It also exacerbates the effects of protein stress when exposed to sewage discharge into natural waters (Pollack et al., 2009).	• At the concentration above PNEC, mortality increases to 33% with 48-hour caffeine exposure (Moore et al., 2008)	• Increased toxicity in fish results in low embryonic development (Lee and Wang, 2015).
vi.	Carbamazepine	• Growth inhibition (Jones et al., 2001).	• Causes inhibition of molting, delayed reproduction, and reduced fecundity in macroinvertebrates, and at high exposure for a longer duration, it acts	• Increases time in Embryonic development of medaka fish (Nassef et al., 2010).

			as an endocrine disrupter in macroinvertebrates (Chen et al., 2019).	
vii.	Ciprofloxacin	• Inhibits the algae growth rate even at low concentrations of ciprofloxacin in water (Ebert et al., 2011).	• Acts as a growth inhibitor and also cause oxidative stress in macroinvertebrates (Dionísio, et al. 2020; Mutiyar and Mittal 2014).	• The function of the cardiovascular system changes in zebrafish. It also acts as a growth inhibitor in fish (Shen et al., 2019).
viii.	Diclofenac	• Inhibition of algal reproduction was observed after 3-5 h of exposure. The toxicity of diclofenac increases sixfold after 53 h of exposure (Schmitt-Jansen et al., 2007).	• Population growth rates show a decrease in macroinvertebrates at an acute toxicity test of 48 h (Lee et al., 2011).	• Effects on the development of immune response in fish. • Alteration in gills and kidneys in fish (Bao et al., 2017; Quinn et al., 2011).
ix.	Ibuprofen	• DNA damage of algae (Vannini et al., 2011).	• Reduces the fertilization success rate of macroinvertebrates (Zanuri et al., 2017).	• Immune system and nephron toxicity effects in fish at 0.1 to 10 µg/L exposure. • Reproduction pattern changes in fish (Mathias et al., 2018; Minguez et al., 2016).
x.	Naproxen	• It adversely affects the cellular ultrastructure that inhibits algal growth (Wang et al., 2020).	• Chronic exposure affects reproduction and decreases population growth rates (Kwak et al., 2018).	• Lowers heart rate egg-hatching inhibition in zebrafish (Li et al., 2016).
xi.	Norfloxacin	• An increase in a concentration above 11.12 mg/l rapidly decreases the growth of algae species and algal cell density (Nie et al., 2009).	• High concentration and exposure time beyond 96 h increases mortality rates and decreases heartbeat. It also decreases average swimming ability and feeding rate (Pan et al., 2017).	• Oxidative stress and immunotoxicity were observed at the early stages of zebrafish (Liang et al., 2020).
xii.	Ofloxacin	• Growth inhibition at a dose of 31.2 µg/L (Ferrari et al., 2004)	• Reduce the fertilization rate and affect reproduction at a dose of 10,000 µg/L (Ferrari et al., 2004).	• Deterioration of cell viability and causes disorders in the immune system, allergic reaction, and tumor formation (Li et al., 2016)
xiii.	Sulfamethoxazole	• Chronic toxicity effects on algae. • Promotes gene expression and changes to algal cell ultrastructure that inhibit cell growth, decrease chlorophyll content, increase cell membrane permeability, and	• Daphnia magna reduces fecundity, decreases ingestion rate, and changes locomotor behavior and metabolic disorder (Zhang et al., 2023).	• Decreases the body length and hatching duration of zebrafish embryos (Liu et al., 2020).

		increase production of reactive oxygen species. (Liu et al., 2020; Xu et al., 2022).		
xiv.	Triclosan	• It causes an increase in mortality rate. Photosynthetic efficiency decreased with increased triclosan concentrations (Ricart. et al., 2010).	• It alters the taxonomic composition and decreases the alpha diversity of macroinvertebrates at a concentration ≥80 µg/L of triclosan (Peng et al., 2014).	• 96 h of exposure causes abnormalities and changes in activity in fish (Liang et al., 2013; Rudel et al., 2013).
xv.	Trimethoprim	• Sensitive to algae and causes growth inhibition starting at low doses and less exposure time (Kolar et al., 2014).	------	• Show genotoxic effects in fish species (Papis et al., 2011).

2.7 Concentration Level of Pharmaceutical Compounds in River Waters

2.7.1 Indian Rivers

In a limited survey from available literature on presence of pharmaceutical compounds in Indian rivers, it was observed that some 13 major rivers have pharmaceuticals in water. The compounds represent four classes of chemicals: antibiotics, NSAIDs, anticonvulsants, and stimulants, as given in Table 2.4.

Table 2.4: Concentrations of pharmaceutical compounds reported in some Indian rivers

S.N.	River	Pharmaceutical Compound(s)	MEC (µg/L)	References
1.	River Kshipra, Ujjain	Norfloxacin*1	1.98	Diwan et al., 2017
		Sulfamethoxazole*1	4.66	
2.	River Akravathi, Bengaluru	Naproxen*1	4.334	Gopal et al., 2020
		Ibuprofen*1	0.105	
		Diclofenac*2	0.041	
3.	River Ganga, Patna	Acetaminophen*2	1.565	Sharma et al., 2019
		Caffeine*4	0.743	
		Ketoprofen*2	0.107	

4.	River Brahmaputra, Guwahati	Caffeine*4	0.410	Kumar et al., 2019
		Acetaminophen*2	0.060	
		Carbamazepine*3	0.008	
5.	River Ahar, Udaipur	Caffeine*4	3.68	Williams et al., 2019
		Ibuprofen*2	1.288	
		Carbamazepine*3	0.57	
		Azithromycin*1	0.41	
6.	River Yamuna, Delhi	Carbamazepine*3	1.386	Mutiyar et al., 2018
		Ibuprofen*2	0.808	
		Acetaminophen*2	0.333	
		Caffeine*4	0.111	
7.	River Cooun, Chennai	Ibuprofen*2	2.320	Subedi et al., 2015
		Amphetamine*4	0.984	
8.	River Yamuna, Agra	Carbamazepine*3	1.850	Jindal et. al., 2015
		Acetaminophen*2	1.55	
		Sulfamethoxazole*1	0.733	
		Diclofenac*2	0.994	
		Naproxen*1	0.423	
		Ibuprofen*2	0.133	
9.	River Yamuna, Delhi	Gatifloxacin*1	4.800	Mutiyar et al., 2014
		Sparfloxacin*1	2.410	
		Cefuroxime*1	1.700	
		Ciprofloxacin*1	1.400	
		Ampicillin *1	1.380	
10.	River Yamuna, Delhi	Amoxicillin*1	8.400	Mutiyar et al., 2013
		Ciprofloxacin*1	1.726	
11.	River Kaveri	Carbamazepine*3	0.002	Ramaswamy et. al., 2011
12.	River Tamiraparani	Carbamazepine*3	0.058	Ramaswamy et. al., 2011
13..		Norfloxacin*1	4.70	Fick et al., 2009
		Ciprofloxacin*1	2500	

	Isakavagu-Nakkavagu Stream of River Godawari, Hyderabad	Trimethoprim*1	4.00	
		Ofloxacin*1	10.0	

*1- Antibiotics; *2- NSAID/ Analgesic; *3- Anticonvulsant, *4- Stimulant

2.7.2 Rivers outside India around the world

The presence of pharmaceuticals has been reported in many rivers worldwide. Table 2.5 presents the reported measured environmental concentration (MECs) of pharmaceutical compounds reported in different rivers worldwide.

Table 2.5: Concentrations of pharmaceutical compounds in some rivers around the world

S.N.	Name of the river	Pharmaceutical Compound(s)	MEC (µg/L)	References
1	River Lambro, Milan, Italy	Amoxicillin*1	51	Riva et al., 2019
		Triclosan*2	0.27	
2	River Ravi, Lahore, Pakistan	Sulfamethoxazole*1	2.7	Khan et al., 2013
3	River Nairobi Basin, Kenya	Sulfamethoxazole*1	13.8	Ngumba et al., 2016
4	River Wangyang, China	Ofloxacin*1	11.8	Jiang et al., 2014
		Sulfamethoxazole*1	13.8	
5	River Mitheu, Ghana	Sulfamethoxazole*1	2.8	Kairigo et al., 2020
6.	River Brisbane, Australia	Sulfamethoxazole*1	2	Watkinson et al., 2009
7.	River Altamaha, USA	Acetaminophen*2	11	Vidal Dorsch et al., 2012
		Naproxen*1	13.1	

*1- Antibiotics; *2- NSAID/ Analgesic

2.8 River Health Assessment Methods

Different biotic species and their distribution in river water establish a relationship to the structure and integrity of aquatic ecosystems (Thomas, 1987). Many Predictive models such as RIVPACS (River Invertebrate Prediction and Classification System) (Wright, 1995), AusRivAS (Australian River Assessment System) (Simpson and Norris, 2000), BEAST (Benthic Assessment of Sediment) (Reynoldson et al., 1997), South African Scoring System (SASS) have been used to understand the biological status of a river. The eco-based index is seen as an instrument for determining the environmental status of rivers (Joshi, 2013; Karr and Chu, 1997).

2.8.1 Ecosystem Health Score (EHS)

Leigh et al. (2012) in their report entitled "Assessment of River Health in the Liao River Basin (Taizi Sub-catchment)," grouped the entire range of indicators into five categories**:**

i. Physicochemical Water Quality Parameters: Among water quality indicators pH, dissolved oxygen (DO), electrical conductivity (EC), suspended solids (SS), total dissolved solids (TDS), anions and cations (K, Ca, Na, Mg, Cl), alkalinity; oxygen demand variables (BOD_5, CODCr, CODMn), Phenols
ii. Nutrients: Ammonium (NH_4), Total Nitrogen (TN), Nitrogen Dioxide (NO_2), Nitrate (NO_3), Phosphate (PO_4), and Total Phosphorous (TP)
iii. Algae: For benthic algae, two indices- The index of biotic integrity (ABI), and the Algae Berger-Parker (ABP) index
iv. Macroinvertebrates: For macroinvertebrates, four indices: total number of taxa (MS), Biological Monitoring Working Party (MBMWP) index, Family level richness of EPT taxa (MEPTS), and Berger-Parker (MBP) index
v. Fish: For fish, Number of individuals (FN), Species-level richness (FS), Fish index of biotic integrity (FBI), Fish Berger-Parker index (FBP)

Based on analyses, they recommended DO, EC, SS, TN, NH_4, TP (6 parameters) for highlands; DO, EC, SS, TN, NH_4, TP, and phenols (7 parameters) for midlands; and DO, EC, BOD_5, CODMn, TN, NH_4, TP and phenols (8 parameters) for lowlands river health assessment. The authors noted that E. coli could be included as an indicator if the program monitored and assessed the river from a human health perspective.

Based on "target" (the guideline representing good health, score 1)" and "critical threshold" (some level of unacceptable health, score 0), site indicator scores (SIS) and IGS were calculated. The overall Ecosystem Health Score was calculated as:

Ecosystem health score = (Physical and chemical score x 2/15) + (Nutrients score x 2/15) + (Algae score x 3/15) + (Macroinvertebrates score x 4/15) + (Fish score x 4/15) -(Eq. 2.3)

The Ecosystem health score ranges between 0 and 1.0. The ecosystem health was classified as critical (EHS < 0.2), poor (≤ 0.4), fair (≤0.6), good (≤ 0.8), and excellent (>0.8). The ecosystem health was schematically presented as a colored pentagon, each of whose five sectors represents the indicator group health score. Red indicates a score of 0–0.2, while green indicates a score of 0.6–1.0 (Leigh et al., 2012).

2.8.2 River Health Index (RHI)

Following a similar analogy of Leigh et al., 2012, Singh and Saxena (2018) proposed a scheme of river health assessment based on the calculation of RHI on a 0-100 increasing scale. Water quality parameters are divided into five indicator groups; two of them from physicochemical characteristics of water, and three based on aquatic species of different trophic levels represented through Algae, Macroinvertebrates (MI) and Fish.

Physicochemical Parameters Indicator Groups

i. **Organo Electrolytic Bacteria (OEB)**: Electrical Conductivity (EC), Dissolved Oxygen (DO), Biochemical Oxygen Demand (BOD), Chemical Oxygen Demand (COD) and Total Coliform (TC).

ii. **Nutrients (NTs)**: Ammonia-Nitrogen (NH3-N), Total Nitrogen (TN), and Total Phosphorous (TP)

Biotic Indicator Groups

For the river environment, three different trophic-level aquatic organisms (Algae, MI and Fish) were considered.

For benthic algae, one index - Genus level Algal Palmer Pollution Index (APPI) was included as representative indicator.

For macroinvertebrates, two indices: i. Shannon Weiner Index (MSW), and ii. Biological Monitoring Working Party (MBMWP) index were included.

For fish, two indices: i. Species-level richness (FS), and Shannon Weiner Diversity Index (FSW) were considered.

The RHI was calculated using Eq. 2.4 as given below:

$$RHI = [(P\&C \times w_1) + (NT \times w_2) + (A \times w_3) + (MI \times w_4) + (F \times w_5)] \times 100 \quad -- \quad (Eq.2.4)$$

P&C: Physical and Chemical group score, NT: Nutrient indicator group score, A: Algal indicator group score, MI: Macroinvertebrate indicator group score, F = Fish indicator group score, and w_1 to w_5 are their respective weightage.

Saxena and Singh (2020) further refined the approach. They used a normalization scheme (Table 2.6) for selected parameters/indices on a 0-5 scale based on a critical concentration (score 0) and acceptable concentration (score 5) to calculate the RHI. RHC is presented through a colored circumscribed pentagon, whose sectors through the center represent one of five indicator groups: i. Organo-electrolytic-bacterial (OEB) qualities. ii. Nutrients, iii.

Algae, iv. Macroinvertebrates, and v. Fish. The color of each sector of the pentagon reflects the health score of the concerned indicator group, and that of the circumscribing pentagon gives the overall RHC at a given location.

Weights of Indicator Groups

After selecting the physicochemical and biotic parameters for RHI calculation, 30% of the weightage was given to physicochemical parameters, such that w_1= 0.15 for OEBs and w_2= 0.15 for NTs. In contrast, biotic indicators were considered long-term integrators of river health, and accordingly 70% of the weightage was assigned to biological parameters, which reflect responses of physicochemical characteristic in river waters. Algae at the lower end of the trophic level have a shorter lifespan than macroinvertebrates, followed by fish (Leigh et al., 2012). Hence, algae were assigned (w_3= 0.20), while MI and fish groups were assigned (w_4=w_5=0.25).

For normalisation of parameters on 0 (Beyond critical) to 5 (within acceptable concentration) scale, Acceptable and Critical concentrations for included parameters were compiled, as given in Table 2.6.

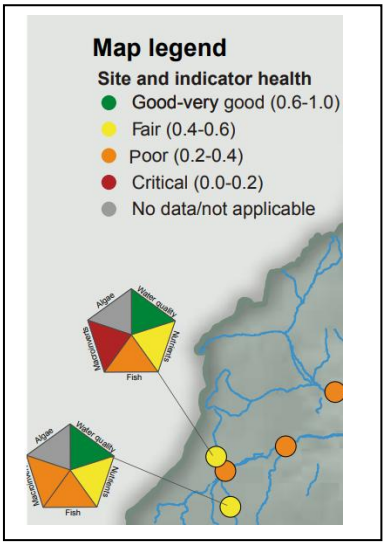
Table 2.6: Acceptable and critical concentrations of physico-chemical and nutrients parameters (Source: Saxena and Singh 2020)

Indicator Group	Parameters	Normalized Score (0-5 scale)		Reference
		Acceptable concentration (5)	Critical Concentration (0)	
1. Physico-Chemical Parameters	i. EC (µmhos/cm)	≤400	>1500	EHMP (2010); Anon (2000)
	ii. DO (mg/L)	≥7	<3	UNECE (1994)
	iii. BOD (mg/L)	≤3	>8	UNECE (1994); CPCB (2015) CPCB (2002)
	iv. COD (mg/L)	≤30	>80	Singh and Saxena (2020)
2. Nutrients (NT)	i. NH_3-N (mg/L)	≤0.3	>1.5	CPCB (2002); MEP (2008)
	ii. TN (mg/L)	≤0.5	>2	Anon (2000); MEP (2003)
	iii. TP (mg/L)	≤0.1	>0.3	CPCB (2002)

The differences in approaches of Ecological Health Score (EHS) as proposed by Leigh et al. (2012) and Saxena and Singh (2020) are presented in Table 2.7. It can be seen that while EHS is on 0 to 1.0 scale, RHI is on 0 to 100 scale. Also, while the EHS categorises the ecosystem health in five classes (Critical, Poor, Fair, Good, and Excellent), RHI divides river health condition (RHC) first into two classes (Acceptable and Poor) and then subdivides these classes into further categories.

Table 2.7: Detailed overview for estimation of ecosystem health

	Source: Leigh et al. (2012)					Source: Saxena and Singh (2020)				
Indicator Group	**P&C**	**NT**	**A**	**MI**	**F**	**OEB**	**NT**	**A**	**MI**	**F**
Weightage	0.14 (w_1)	0.14 (w_2)	0.20 (w_3)	0.26 (w_4)	0.26 (w_5)	0.15 (w_1)	0.15 (w_2)	0.20 (w_3)	0.25 (w_4)	0.25 (w_5)
Parameters Considered	DO BOD_5 CODMn EC Phenols	TN TP NH_4	ABI2, ABP	MS, MBMWP, MEPTS MBP	FN, FS, FBI, FBP	EC, DO, BOD, COD, FC	NH_3-N, TN TP	APPI	MSW MBMWP	FS FSW
Normalization Scale of Parameters	0 to 1	0 to 1	0 to 1	0 to 1	0 to 1	0 to 5	0 to 5	0 to 5	0 to 5	0 to 5
Nomenclature used	Ecosystem Health Score Scale: 0-1.0	Ecosystem health score: >0.8: Excellent > 0.6 ≤ 0.8: Good ≤ 0.6: Fair ≤ 0.4: Poor < 0.2: Critical				River Health Index (RHI) Scale: 0-100		River health condition classification: **Acceptable**: >80: Excellent 70-80: Very Good 60-70: Good **Poor**: 50-60: Stressed 40-50: Over Stressed 20-40: Critical ≤20: Sick/Dead		



Fig, 2.2 (a) Color coded Ecological Health Pentagonal Map of the Lio River Basin, China, based on Ecological Health Score (Leighi et

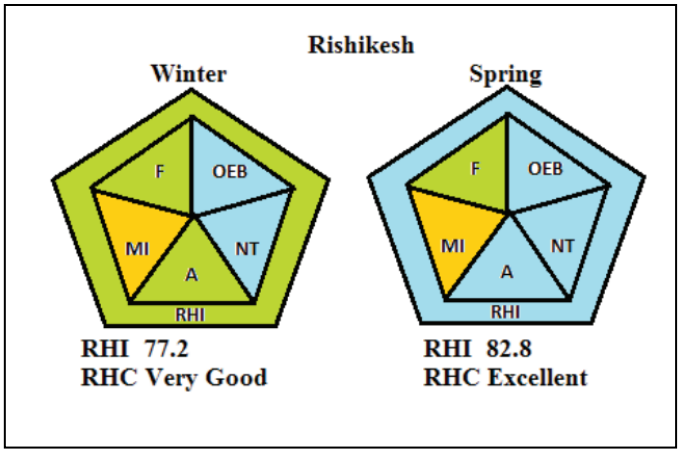


Fig. 2.2 (b) Color coded RHC Pentagonal Map for the River Ganga near Rishikesh based on IGS and RHI (Saxena and Singh, 2020).

2.9 Review of Wastewater Treatment Technologies for Improving Water Quality

The concentration of PPs in hospital wastewater is 4-150 times higher than in domestic wastewater (Hocquet et al., 2016; Mesdaghinia et al., 2009) and is only partially treated in conventional wastewater treatment. WHO (2016) reports that treating PPs from wastewater to reduce ABRB in rivers may cost the global economy as much as $ 100 trillion.

2.9.1 Conventional Wastewater Treatment Technologies

Conventional treatment technologies degrade only 18-25% of the pharmaceuticals from wastewater (Kodam et al., 2021; Castiglioni et al., 2006; Lishman et al., 2006; Paxeus, 2004; and Santos et al., 2007). STPs are often strategically located near rivers to treat municipal and industrial wastewater before discharging the treated effluent into the river. These plants help reduce pollution and ensure compliance with environmental standards.

Treating PPs at sources near pharmaceutical manufacturing industries or HWW reduces the pollutant load reaching the nearby river. Existing WHO guidelines suggest that the disposal of HWW should be regulated through on-site treatment, requiring primary, secondary, and tertiary treatments. For effective river health improvements, the priority remains on treating pharmaceutical wastewater to reduce the load of PPs in aquatic environments.

Different existing technologies near banks of rivers, including other biological treatment, with the role of tertiary treatment technologies options for reducing the load under acceptable concentrations, have been discussed in detail:

2.9.1.1 Activated Sludge Process (ASP)

The activated sludge process is aerobic and uses the microorganisms still suspended to treat wastewater. Three main parts make up the process: an aeration tank, where raw wastewater is introduced and mixed with air in a continuous flow, plug flow, or tapered flow form of aeration; a secondary clarifier, where the activated solids are separated from the effluent by settlement; and return activated sludge equipment, which pumps the activated sludge

back to the initial tank for aeration and re-seeding the incoming raw wastewater, as well as achieving the necessarily mixed liquor suspended solids concentration to aid in the breakdown of organic matter, which is a mixture of raw sewage and activated biological floc. The excess sludge is wasted when the initial tank's MLSS concentration surpasses the desired level. The system maintains the food-to-microorganisms (F/M) ratio to stop the filamentous growth of microorganisms that would cause the bulking of the sludge (Sastry et al., 2013). The process flow diagram for ASP is shown in Figure 2.3.

In ASP, the process for removal of PPs such as sulfamethoxazole and other compounds, including ibuprofen, triclosan, etc., may be enhanced using a combination of different microbial species and specific enzymes (such as monooxygenase and dioxygenases). Also, an increase in sludge retention time (SRT) from 6 to 54 days was observed to enhance removal efficiency from 30% to 70% (Fischer et al., 2014).

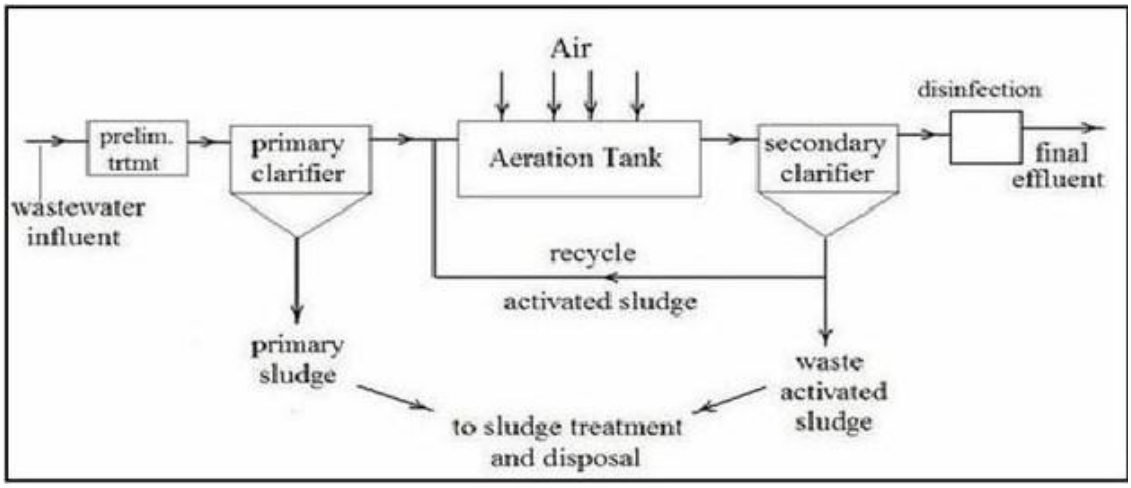


Fig: 2.3 Schematic Representation of ASP (Source: Sastry et al., 2013)

2.9.1.2 Sequencing Batch Reactor (SBR)

SBR technology is a modified form of ASP. SBR works in batch mode, with all biological and physical processes occurring in the same basin sequentially. There are four stages to this process: filling, where raw wastewater is poured into the basin in batches; reaction, where air is added and mixed with the wastewater; settling, where the

solid and liquid phases are allowed to separate; and decanting, where the treated wastewater is extracted from the basin. For SBR to function, at least two basins are needed, one in the reaction phase and the other in the settling and decanting conditions. Better sludge-settling properties increase efficiency in the process (Mace et al., 2002). Antibiotics such as ciprofloxacin, sulfamethoxazole, and trimethoprim get removed from SBR by 20-30%, while compounds under NSAIDs (ibuprofen, naproxen, and diclofenac) have 10-30% efficiency for removal from water (Tian et al., 2023). Tertiary treatment is required to increase the removal efficiency from wastewater.

The process flow diagram for SBR is displayed in Figure 2.4.

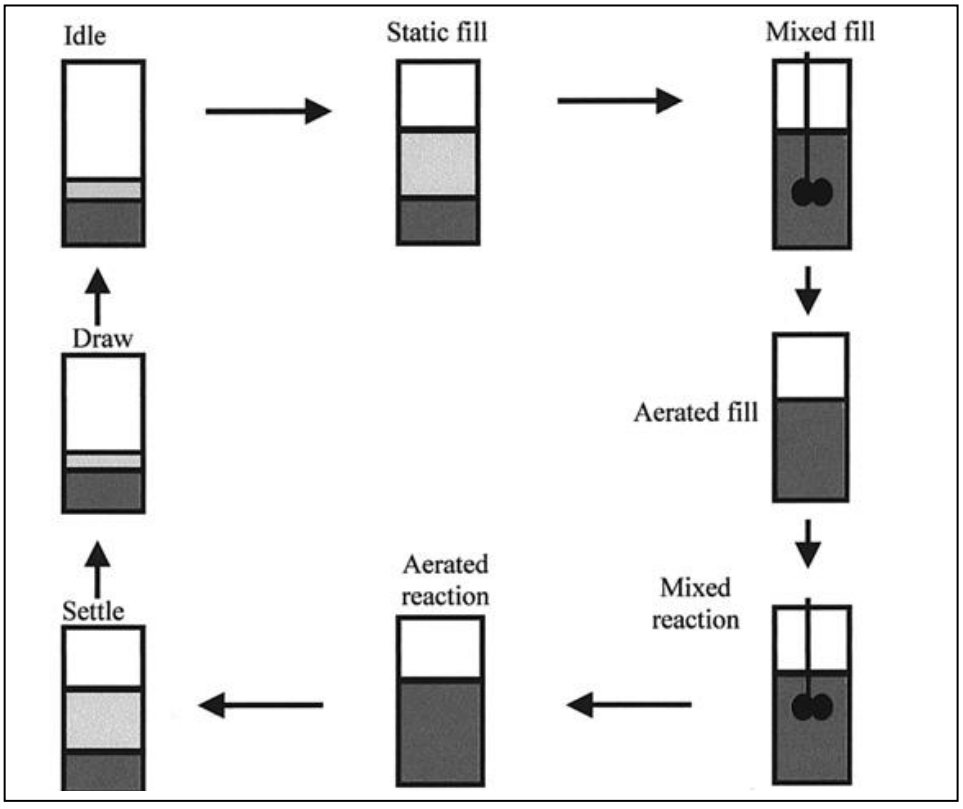


Fig: 2.4 Schematic Representation of SBR (Source: Mace et al., 2002)

2.9.1.3 Anaerobic- Anoxic -Oxic (A2O) Process

The A2O treatment method is an advanced adaptation of ASP, primarily focused on increasing the removal of nutrients, specifically nitrogen and phosphorus. The procedure begins with ingesting wastewater into an anaerobic tank, where microorganisms stimulate

to emit phosphorus in ortho-phosphates without oxygen. The subsequent tank is anoxic and devoid of oxygen, where microorganisms utilize energy from nitrates within the wastewater derived from the oxidation of ammoniacal-nitrogen to nitrate form in the aerobic tank. The nitrified liquid is then recirculated back into the anoxic tank. In the aerobic tank, active phosphate accumulating organisms absorb dissolved ortho-phosphates and convert them into polyphosphates, which do not dissolve in water. This undissolved biomass is later extracted through the secondary clarifier, necessitating a sludge thickener.

NSAIDs (ibuprofen, diclofenac, and naproxen); antibiotics (ciprofloxacin, sulfamethoxazole, erythromycin), anticonvulsants (carbamazepine, lamotrigine) are the different classes of PPs with removal efficiency less than 10% from hospital wastewater (Park et al., 2017; Gallardo et al., 2018).

The diagram illustrating the A2O process is presented in Figure 2.5.

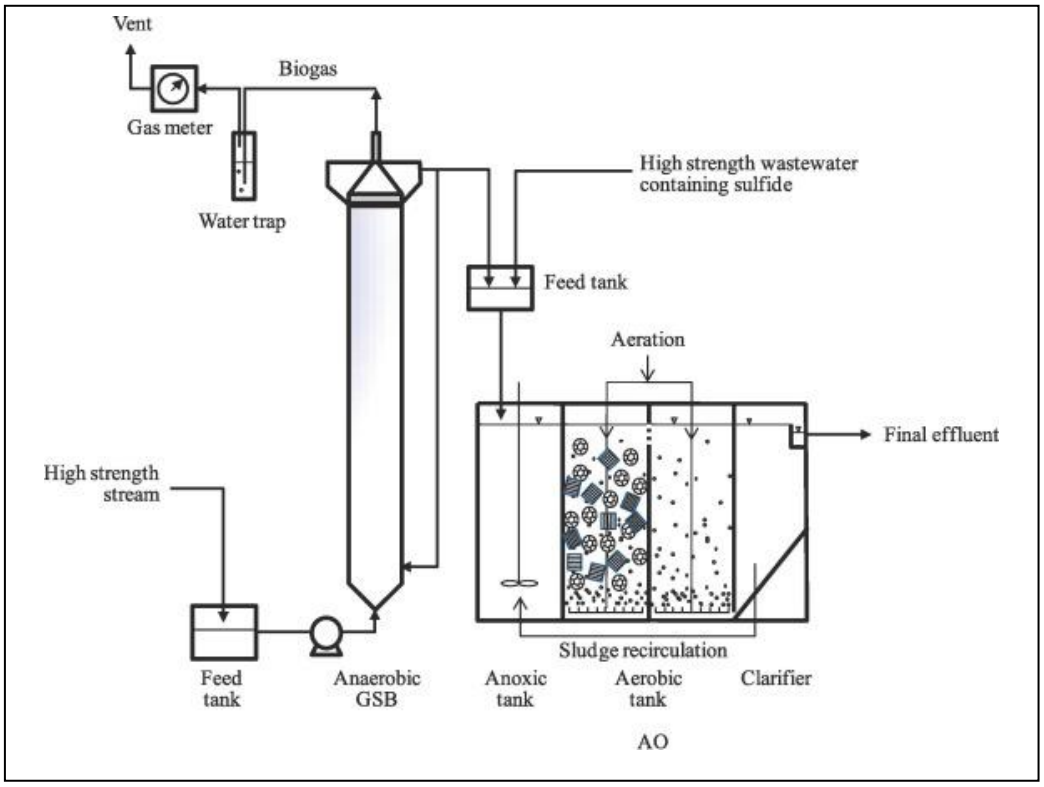


Fig: 2.5 Schematic Representation of A2O (Source: Gallardo et al., 2018)

2.9.1.4 Upflow Anaerobic Sludge Blanket (UASB)

The up-flow anaerobic sludge blanket reactor, a suspended growth process, directly influences the reactor from the bottom and stirs the settled activated sludge blanket, causing mixing and the removal of organic matter from the system. As a result of the technology, energy is saved and no additional equipment is needed to mix the sludge with the influent. While the gas generated is collected, the reactor's top section removes the effluent. The anaerobic nature of UASB renders the effluent unstable and unsuitable for discharge into the river system due to its high immediate oxygen demand. In order to stabilize the effluent produced, an aeration tank that runs in extended aeration mode follows the reactor. The prolonged aeration phase biomass is in the endogenous respiration phase, with a high air supply and low F/M. This results in stabilized sludge forming, further settling in the secondary clarifier. Among PPs, literature suggests 20-60% removal of antibiotic and NSAIDs class pollutants, while anticonvulsants have less than 20% removal efficiency from wastewater. Figure 2.6 shows a schematic representation of the UASB process.

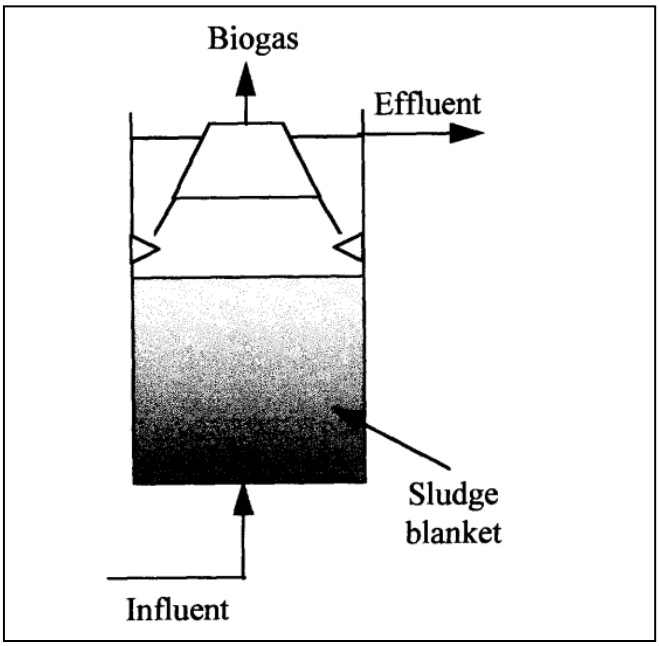


Fig: 2.6 Schematic Representation of UASB (Source: Seghezzo et. al., 1998)

2.9.1.5 Moving Bed Biofilm Reactor (MBBR)

Wastewater is treated using patented media in suspension form under aerobic conditions. The biomass cultivated on the media surface breaks down the organic matter through an attached growth process, which is the effluent. Due to the plastic media's tendency to float and its lighter weight, air diffusers on the reactor's sides aid in downward mixing. While the inner layer of the biomass attached to the media is in the anoxic phase and performs denitrification, the biomass on the media's periphery carries out the nitrification process. Mechanisms such as biodegradation, sorption to biofilm, and co-metabolism are the main principles for pharmaceutical removal, which resembles the MBBR technology and results in the removal of organic pollutants from hospital wastewater. The study suggests that integrating tertiary treatment can enhance the removal of pharmaceuticals by more than 90% (Ooi et al., 2018; Khan et al., 2023).

Figure 2.7 shows a schematic representation of the flow, as depicted in Figure 2.6.

Removal efficiency of conventional STPs by various wastewater treatment technologies is summarised in Table 2.8

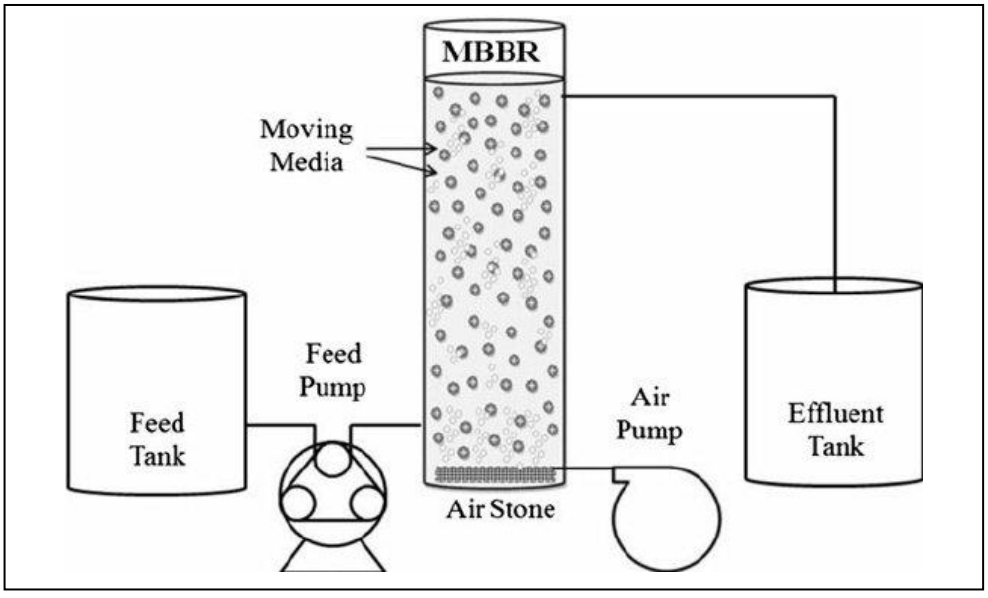


Fig: 2.7 Schematic Representation of MBBR (Source: Nakhli et. al., 2014)

Table 2.8 Treatment technology and removal efficiency of conventional STPs

Treatment Technology	Monitoring parameters and initial concentration (µg/L)	Removal Efficiency	Major Observations	References
1. Activated Sludge Process (ASP)	COD/TOC/NH_3-N Ketoprofen (0.6) Diclofenac (0.1) Azithromycin (1.5)	>50 > 45	• ASP + Biofilm ultrafiltration with dissolved oxygen 1-4.5 mg/L	Mousaab et al., 2015
	BOD COD Ciprofloxacin (7.573) Ofloxacin (4.662)	50-60 45-65 56 34	• Good removal of BOD, COD of HW reported with HRT of 24 h	Shokoohi et al., 2017
	Ciprofloxacin (<1) Caffeine (75) Carbamazepine (<1) Sulfamethoxazole (<1)	90 Up to 90 80 55	• Aerobic Tank followed by sand filtration and chlorination.	Qarni et al., 2016
	Ciprofloxacin (42.8) Ibuprofen Diclofenac Sulfamethoxazole (23.5) Trimethoprim (2.8)	45 Negative Removal Negative Removal >50 >50	• ASP followed by filtration`	Lien et al., 2016
2. Sequencing Batch Reactor (SBR)	Caffeine (0.13) Acetaminophen (0.15) Carbamazepine (0.16) Thiabendazole	>80 >80 <10 <10	• Removal efficiency increases after addition of UV disinfection	Bhattacharjee et al., 2024
	Ibuprofen (41.22) Ketoprofen (2.01) COD NH_3-N	87 88 88 89	• 24-hour HRT • Experiment carried on Hospital Wastewater	Alattabi et al., 2015
3. Anaerobic-Anoxic - Oxic (A2O) Process	Acetaminophen (8.6) Ibuprofen (8.716) Naproxen (5.2) Ketoprofen Diclofenac (2.495)	>80 40 47 5 6	• HRT= >10 days • Influenced by Mycolata bacteria	Gallardo-Altamirano et al., 2019
	Ketoprofen (2.3) Diclofenac (1.7) Naproxen (5.9)	73 <10 23-47	• Suggests low capability in pharmaceutical removal.	Park et al., 2017
4. Upflow Anaerobic Sludge	Tetracyclines (1740) Sulfamethoxazole (2560) Ampicillin (345)	>80	• Biodegradation and adsorption to sludge reduced the concentration.	Hou et al., 2019

Blanket (UASB)				
	Sulfamethoxazole (85) COD (198)	52 26	• At pH> 5 • High COD load	Chen et al., 2018
5. Moving Bed Biofilm Reactor (MBBR)	BOD, COD, NH_3-N Azithromycin (25) Trimethoprim (18) Sulfamethoxazole (20) Tramadol (16)	25-65 30 20 20 Negative removal Negative remo	• MBBR with three identical reactors with HRT= 6h in each reactor.	Casas et al., 2015
	Sulfadiazine (8) Ibuprofen (6) Sulfamethoxazole (12) Trimethoprim (3)	9 >25 >25 30-35	• MBBR with six reactors. • HRT = 1-2 h.	Ooi et al., 2018

2.9.2 Tertiary Treatment Methods: Advanced Oxidation Processes (AOPs)

The ASP or SBR is the most commonly used method of sewage treatment. It generally includes a preliminary treatment phase, a primary settling tank, an aerobic degradation stage, and a secondary settling tank. The treated secondary effluent is often chlorinated before being released into a water body. The need for tertiary treatment is necessitated for load reduction of other parameters not treated up to the secondary level of treatment. Water quality under NTs and PPs groups of indicators require additional interventions for river health improvements. Among different options for tertiary treatment, application of advanced oxidation processes (AOPs) and constructed wetlands (CWs) are most commonly recommended. Augmentation of existing facilities with AOPs is the most important, promising, efficient, and eco-friendly method suggested to remove residual organic pollutants from water and wastewater due to their chemical stability, technical efficiency, and environmental impact (Gaur et al., 2018; and Sun et al., 2020). AOPs are typically divided into two categories based on their activation mechanism: photochemical and thermal (non-photochemical) (Kanakaraju et al., 2018). AOPs such as the Fenton

process, UV radiation, ozonation, chlorination, and hydrogen peroxide are methods that generate OH radicals to adequately oxidize organic pollutants (Hassanshahi and Karimi-Jashni, 2018; Park et al., 2019), and pollutants are fragmented into harmless end products such as CO_2 and H_2O. A detailed discussions on treatment options under AOPs are discussed below:

2.9.2.1 Ozonation

Ozonation uses ozone as an oxidizing source to degrade pharmaceuticals and other organic pollutants of concern. It decomposes to generate hydroxyl radicals, which are generally highly reactive for target compounds with aromatic rings, double bonds, and other functional groups like phenols and amine (Tambosi et al., 2009; Gerrity et al., 2011; Khan et al., 2020). The iodometric method, which gathers the ozone generators, is used in ozone pilot plants to produce ozone. An oxygen cylinder and a liquid/gas column with a portable pump for water circulation in the column are necessary for ozone formation. After the gas is injected through a porous diffuser, ozone is formed in the column. Gerrity et al. (2011) examined the ozonation process for treatment of PPs and reported >90% removal of paracetamol, diclofenac, and sulfamethoxazole. The process effectively removes PPs from HWW by more than 76% at an ozone dose of 3.5- 17.0 mg /L at pH> 8; the decomposition rate increases with an increase in pH (Khan et al., 2020).

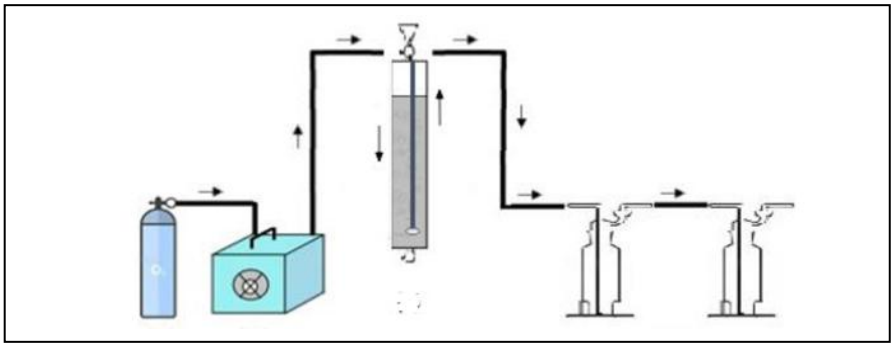


Fig: 2.8 Schematic Representation of Ozonation (Source: Costa et al., 2023)

2.9.2.2 Chlorination

Chlorination is a wastewater treatment method with high inactivation capability and comparatively low cost, making it a widespread disinfection and sterilization technique (Dodd, 2012). In wastewater and drinking water purification, free available chlorine, commonly used as elemental chlorine (Cl_2), sodium hypochlorite (NaOCl), or calcium hypochlorite ($Ca(OCl)_2$), is the most widely used disinfectant (Dodd, 2012). As a strong oxidizer, chlorine reacts with organic compounds, which leads to the formation of harmful chlorinated byproducts with negative effects on human health (Albolafio et al., 2022). Chlorination has no effect on NTs indicator group of parameters, which makes it an inappropriate selection to provide treated wastewater to waterbody susceptible to eutrophication. On the other hand, chlorine can easily oxidize pharmaceutical compounds. Li and Zhang (2011) reported a reduction rate of 53 to 83 percent in the removal of pharmaceutical compounds, including erythromycin, tetracycline, trimethoprim, ciprofloxacin, norfloxacin, and sulfamethoxazole. It is a more economical and ecologically sustainable method with low greenhouse gas emissions and minimal energy requirements (Zhuang et al.,2015; Tak and associates. 2017).

2.9.2.3 Ultraviolet (UV) Irradiation

UV irradiation is an advanced process used for sterilization and disinfection. It functions effectively at wavelengths ranging from 100 to 1000 nm. UV light degrades pharmaceutical pollutants through photolytic and photocatalytic processes, breaking their chemical structures and dissociating them into low-end by-products noncorrosive to water (Huang et al., 2014; McKinney and Pruden, 2012). The removal efficiency of pharmaceuticals via UV irradiation is influenced by key operational parameters, including UV dose, wavelength, retention time, and water flow rate. Enhanced removal efficiency has been observed when UV is coupled with other AOPs. For instance, integrating UV with H_2O_2 technology achieved 94% efficiency in removing 20 pharmaceuticals (Chin et al., 2005). Specific

combinations, such as UV/H_2O_2, have demonstrated high removal rates. A complete reduction (100%) of pharmaceuticals like diclofenac, sulfamethoxazole, and norfloxacin was achieved using UV irradiation with H_2O_2 (Tambosi et al., 2009; Rosario-Ortiz et al., 2010). Similarly, coupling UV with photo-Fenton (Fe^{2+}) and H_2O_2 technologies eliminated diclofenac, triclosan, and sulfamethoxazole (Cruz et al., 2013).

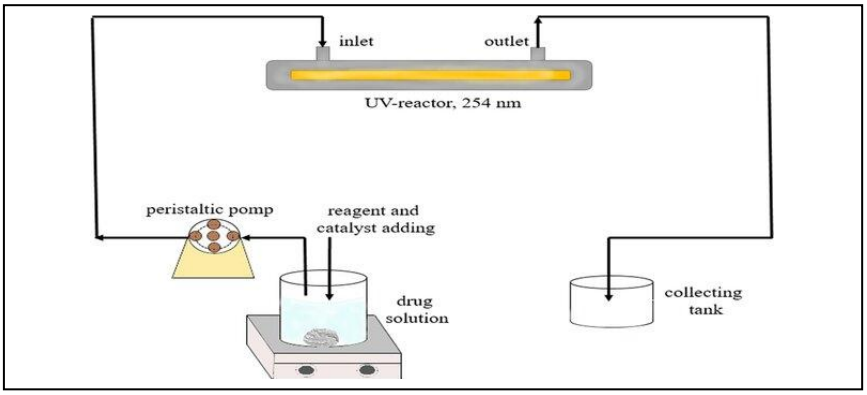


Fig: 2.9 Schematic Representation of ultraviolet (UV) light irradiation (Odabaşi et al., 2022)

2.9.2.4 Hydrogen Peroxide (H_2O_2)

Hydrogen peroxide is utilized as an oxidizing agent, a bleaching substance, and a disinfectant, breaking down into H_2O and O_2 without leaving behind harmful byproducts. When used as a co-oxidant in the ozonation process, hydrogen peroxide reacts with ozone to enhance the formation of hydroxyl radicals. For every three O_3 molecules needed for one HO-, hydrogen peroxide allows one ozone molecule to generate a single hydroxyl radical (Acero and von Gunten, 2001). The decomposition of H_2O_2 to yield •OH is facilitated by ozone, ultraviolet (UV) light, or the photo Fenton process (Fe2+) (Jung et al., 2012). PPs of deep concern for aquatic organisms, such as carbamazepine, acetaminophen, diclofenac, and trimethoprim, were reported to have a reasonable removal probability above 90% with a combination of either ozone+ H_2O_2 or H_2O_2 + UV (Rosario -Ortiz et al., 2010; Gerrity et al., 2011).

Table 2.9: AOPs-based Treatment technologies and removal efficiency for PPs

Treatment Technology	Monitoring Parameters and initial concentration (µg/L)	Removal Efficiency (%)	Major Observations	References
Ozonation+ H_2O_2	Carbamazepine Ciprofloxacin Naproxen Paracetamol (6)	>95	• Dose of ozone= 1.2 mg/L • Retention Time= 10 minutes • Ratio= O3/ CBZ=10	Andreozzi et al., 2003
Ozonation	Sulfamethoxazole (0.6 Carbamazepine (2.4) Diclofenac (1.4)	>90	• Dose=5-15 mg/L • Retention Time= 20 minutes	Ternes et al., 2003
Ozonation	Carbamazepine Diclofenac Ibuprofen Sulfamethoxazole	.>90	• Dose= 0.2- 6 mg/L • Retention Time= 10 minutes • pH. 9	Huber et al., 2003
Ozonation	Carbamazepine (1) Diclofenac (1) Ibuprofen (1)	>76	• Ozone Dose: 3.5-17.0 mg/L	Khan et al., 2020
Ozonation+H_2O_2	Carbamazepine (1.80) Diclofenac (1.65) Sulfamethoxazole (4.43)	>90	• Among AOP removal of pollutants from wastewater by ozone, ozone + H2O2, and UV +H_2O_2 are best for PPs removal.	Gerrity et al., 2011
Ozonation	Sulfamethoxazole (6980) Diclofenac (4880) Carbamazepine (6150)	51 73 59	• Dose= 5g/h • Retention time= 40minutes • Single dose	Naddeo et al., 2015; and Guo et al., 2020
UV	Ciprofloxacin (1210-9450)	45-63	• Time 120minutes	Mondal et al., 2018
UV+ Chlorination	Naproxen (11)	>98	• Retention Time= 9 minutes	Liu et al., 2019
UV+H_2O_2	Trimethoprim (0.235) Carbamazepine (1.038) Diclofenac (0.605) Sulfamethoxazole (1.638)	>80	• 0.11mg H_2O_2mg/ TOC	Justo et. al., 2013

O_3+UV	Amoxicillin (231) Sulfamethoxazole (4.5)	>90- 94	• Retention Time= 20 minutes • Ozone dose= 12.77 mg/min • pH= 3-4.8	Silva et. al., 2022

2.9.3 Biological Approach for Tertiary Treatment of Wastewaters

2.9.3.1 Membrane Bioreactor (MBR)

Low-pressure microfiltration membranes with sizes ranging from 0.1 to 0.4 μm are used in membrane bioreactors. The membrane aids in the liquid-solid separation process, and the biomass is present in suspension form. The reactor has anoxic and aerobic zones, and the membrane is positioned in the former. Liquids and biosolids are filtered and separated by suction pumps to remove mixed liquor from membranes. Installed at the bottom, air diffusers continuously push liquid and air to remove the membranes. MBR technology efficiently lowers suspended solids (SS), organic pollutants, and pathogens, mainly through photodegradation, biodegradation, sludge, and volatilization. Khan et al. (2020) reported the removal efficiency of 50-90% for PPs such as diclofenac, ibuprofen, carbamazepine, and ofloxacin by MBR technology. The removal efficiency in MBR technology depends on hydraulic retention time (HRT) and sludge retention time (SRT). Some of the PPs, such as ibuprofen and carbamazepine, get entirely removed by MBR technology (Khan et al., 2020). Tambosi et al. (2009) recommended MBR technology in combination with an AOP (H_2O_2/ UV+O_3), which could remove PPs up to 80-90 % from HWW. Recently, Vo et al. (2019) suggested using MBR combined with ozonation as a potential technology to remove PPs from wastewater. Additionally, Figure 2.10 displays the MBR process flow diagram.

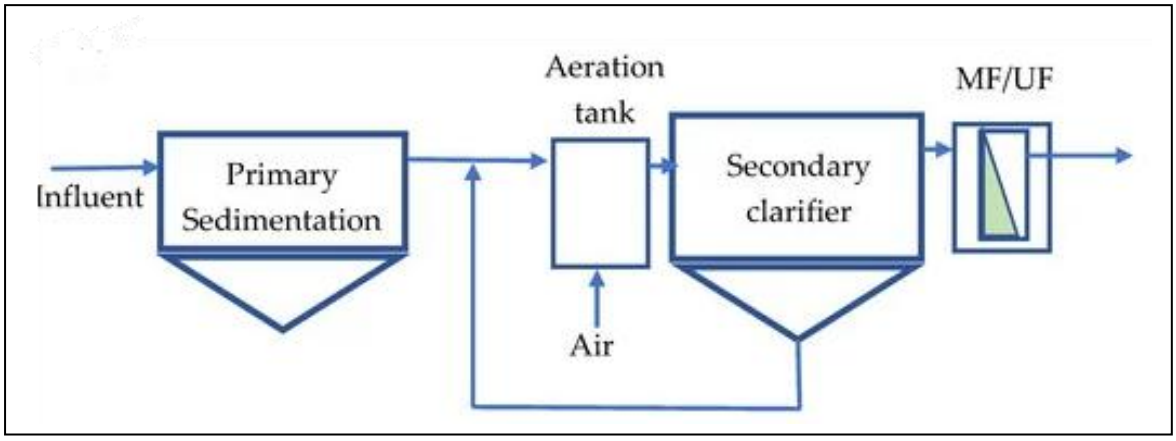


Fig: 2.10 Schematic Representation of MBR (Source: Rahman et al., 2023)

2.9.3.2 Constructed Wetlands (CWs)

CWs generally use three treatment configurations: 1. Horizontal flow, 2. Vertical flow, and 3. Hybrid (combination of horizontal and vertical flows) removes conventional and PPs of concern (Resende et al., 2019). Treatment technologies with low energy consumption and high

removal efficiency of PPs, including ABRB should be preferred. Biological treatment methods using constructed wetlands have been found to show high removal efficiency of PPs and ABRB

from the aquatic environment (Alam et al., 2021; Liu et al., 2019; Dires et al., 2018; Rizzo et al., 2013; Sidrach-Cardona, 2013; Threedeach et al., 2012). Dires et al. (2018) evaluated the

removal of ABRB by surface flow CW at a pilot scale and reported ABRB reduction of 94% in vegetated CW. E. coli and Salmonella isolates were reported to be resistant to PPs such as ampicillin, doxycycline, erythromycin, cefoxitin, and chloramphenicol. Sidrach-Cardona (2013) also observed that CWs remove indicator, pathogenic, and ABRB more efficiently than conventional WWTPs. CWs have also been reported as the best-suited 'engineered natural wastewater treatment system' for removing conventional water quality

parameters such as BOD_5, COD, NH_3-N, TN, and TP. It is also effective in the natural mechanism to photodegrade PPs by supporting reactive oxygen species from sunlight (Mestre et al., 2019). Khan et al. (2020) reported removal efficiency of BOD_5 (56-96 %), COD (65-93 %), and PPs such as diclofenac, ofloxacin, and ciprofloxacin from hospital wastewater up to 65 % by using CW with aeration. The addition of aeration in planted and unplanted setups increases the removal efficiency of pharmaceutical compounds such as acetaminophen, ciprofloxacin, caffeine, diclofenac, and ofloxacin from hospital wastewater (Khan et al., 2020; and Conkle et al., 2008). Vertical and surface flow CW with HRT from 5 -15 days show an increase in the removal efficiency of conventional parameters up to 91% while that for PPs increases up to 50-80% for diclofenac, carbamazepine, 85 % for acetaminophen, 90% for ibuprofen, ketoprofen, 97% for naproxen, and 99 % for caffeine (Vo et al., 2019; Chen et al., 2016; and Llorens et al., 2009).

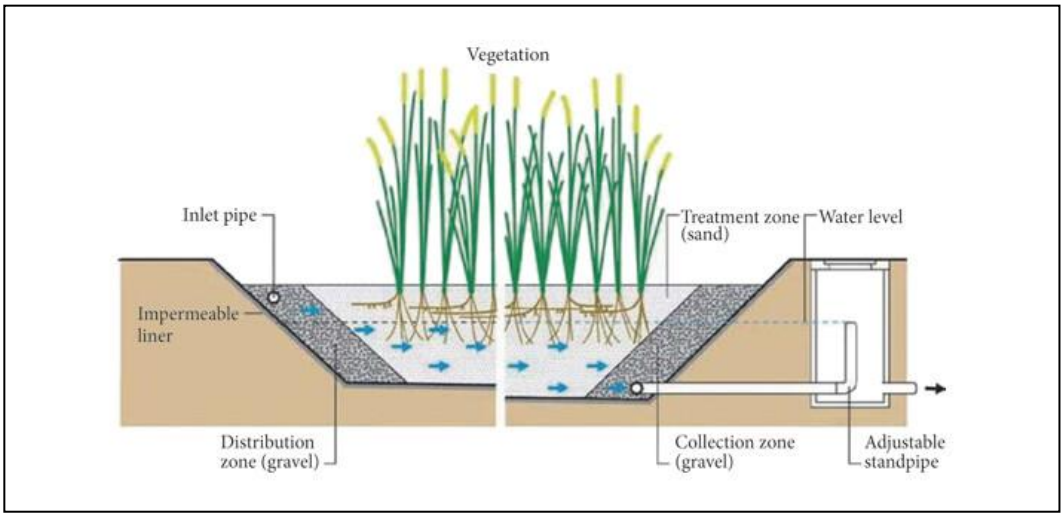


Fig: 2.11 Schematic Representation of CW (Source: Makopondo et al., 2020)

Table 2.10: Treatment technology and removal efficiency for biological methods of tertiary treatment

Treatment Technology	Monitoring parameters and initial concentration (µg/L)	Removal Efficiency (%)	Major Observations	References
1. Membrane Bioreactor (MBR)	Ibuprofen (4150) Carbamazepine (3650) Ofloxacin (3250) Erythromycin (2560)	>90 >90 50 <50	• MBR packed with activated carbon and MBR + UV recommended for HW.	Khan et al., 2020
	BOD, COD, Carbamazepine (5.90) Naproxen (4.8) Sulfamethoxazole (8.45)	90 30 Negative removal 20	• MBR followed by UV	Kohler et al., 2012
	BOD, COD NH_3-N Roxithromycin (55) Sulfamethoxazole (48) Trimethoprim (51)	57-80 45-70 55-85 65-85 40-90	• Recommended combination of MBR+H2O2/UV/+O3 for 12-100% removal efficiency.	Tambosi et al., 2009
	BOD COD NH_3-N	>85 >70 40-60	• The recommended combination of MBR + chlorination for removal efficiency up to 95%. It also reduces pathogenic bacteria, E. coli.	Liu et al., 2010
	Amoxicillin (33) Ciprofloxacin (6000) Sulfamethoxazole (1200)	30-35	• MBR + 450 mg/ L of PAC with HRT of 4 days.	Nielsen et al., 2013
	Azithromycin (0.139) Diclofenac (0.833) Carbamazepine (0.222) Ciprofloxacin (31.98) Norfloxacin (5.933) Trimethoprim (0.930)	21 3 8 51 1 47	• Primary clarifier followed by MBR	Kovalova et al., 2012
2. Constructed Wetland (CW)	BOD COD Diclofenac (4670) Ofloxacin (7640)	56-96 65-93 >65 50-60	• Aeration increases the removal efficiency compared to planted and unplanted setups. • Plant used: Phragmites Australis.	Khan et al., 2020
	NH_3- N, TN Acetaminophen (10000)	>50-75 > 85	• Vertical flow CW with 5 d HRT. • Material used: sand, pea gravel, and gravel. • Plant species: Surpus Validus.	Vo et al., 2019

	Naproxen (2.20) Diclofenac (4.5) Caffeine (1000) BOD_5 COD TSS NH_4-N TP	76–97 17–48 93–99 87 75 91 46 37	• Vertical flow CW with 1 week HRT. • Material used: sand, gravel (Size: 4-8mm) • Plant species: Phragmites.	Chen et al., 2016
	TSS, COD, and NH_4 Ibuprofen (0.07) Ketoprofen (2.8) Naproxen (0.40) Diclofenac (1.36) Carbamazepine (0.45)	80-85 >90 >95 50-80 >85 < 40	• Surface flow CW, HRT: 5-15 days • Material used: Sand, Gravel • Plant Species: Typha Latifolia, Phragmites Australis.	Llorens et al., 2009
	Ibuprofen (0.90) Naproxen (0.90) BOD TSS NH_3-N	97 >95 60-85 60-85	• Horizontal subsurface CW Biofilters and two biological sand filters are used to increase efficiency.	Matamoros et al., 2009
	Caffeine (0.002) Acetaminophen (0.017) Carbamazepine (0.003) Sulfamethoxazole (0.007)	>90 >90 50 <50	• Vegetated vertical flow-constructed wetlands with unsaturated flow and better oxygenation effectively remove PPs.	Conkle et al., 2008

2.9.4 Innovative Approach for RHC improvements: Source Separation of Urine

Based on the estimate of average excretion and food supplied to the Swedish population, according to the free ammonia statistics and on statistical analysis of different foodstuffs, relationships have been developed between the food supplied according to free ammonia and the excretion of N and P. The amount of nitrogen in urine is linearly correlated with its protein content. As per Jönsson and Vinnerås' (2004) study, generally, the amount of protein in food is calculated from analyses of its nitrogen content. Therefore, the nitrogen and other nutrient content of the excreta was calculated from the protein content of the food supply

$$N = 0.13 \times (\text{Total protein intake}) \quad \text{Equation 2.5}$$

$$P = 0.011 \times (\text{Total protein intake}) \quad \text{Equation 2.6}$$

$$K = 0.049 \times (\text{Total protein intake}) \quad \text{Equation 2.7}$$

The following equations give approximate data with fewer variations when compared to several studies.

$$Average\ Protein\ Intake = \frac{(Urban\ Population \times Urban\ Intake) + (Rural\ Population \times Rural\ Intake)}{Total\ Population}$$

As per the Ministry of Statistics and Programme Implementation, GoI, the national nutritional intake in urban areas is 60 g/day/ capita, while in rural areas it is 56 g/day/ capita. The separation of nitrogen from the wastewater stream may be estimated using such relationships.

2.10 Identification of Research Gaps

From the available literature, it is observed that the toxicity of PPs on aquatic organisms has been assessed using risk assessment methodologies such as risk quotient (RQ), hazard quotient (HQ), and optimized risk quotient (RQ_f). Up to MEC= PNEC (RQ=1), there seems 'low risk' to different trophic levels of aquatic organisms, such as algae, MI, and fish. 'High risk' conditions start once RQ>1.

Many rivers in India and around the world have been reported with PPs above PNEC, suggesting ecologically 'high risk' conditions to biotic indicators. There is very limited information available for such ecologically 'high-risk' conditions on biotic indicators and overall river health.

In river health assessment methods, there is virtually no framework that includes the effects of PPs in water and the consequential effects on aquatic organisms.

Also, as the conventional methods of wastewater treatment are reported to be not very efficient in the removal of PPs from water streams, there is an urgent need to examine tertiary treatment methods for river health restoration programs.

2.11 Scope of the Present Study

This study aims to develop a river health assessment framework, including the effects of PPs on biotic indicators of the aquatic environment. It is desired to produce a color-coded pictorial representation of river health conditions to support the river managers and policymakers for scientific and purposeful intervention toward river health restoration.