

REVIEW / ARTÍCULO DE REVISIÓN

A review on emerging micropollutants: sources, environmental concentration and toxicity

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DOI. 10.21931/RB/2021.06.04.29

Abstract: Every minute, the environment is filled with pollutants of various types, including physical, chemical, and biological. A new threat has emerged in recent years due to human activity, which is of significant concern. These pollutants are not like conventional pollutants but can alter the physiology of living things, and hence these are named emerging pollutants. The pollutant sources include crop protection chemicals, personal care products, antimicrobial mixtures, active pharmaceutical ingredients (API). These compounds are biologically crucial because their minute quantity can also disrupt an individual's endocrine system, and hence they are also called endocrine disruptors. This current work reviews many aspects, including source, problems, and legislative solutions that have been farmed to cope with the current situation of emerging micropollutants.

Key words: Emerging pollutants; chemicals, Active pharmaceutical ingredients (API), endocrine disruptors, microplastics.

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Introduction

Micropollutants are chemical compounds usually found in lower concentrations in the aquatic environment^{1,2}. Their amount in water may be significantly from undetectable to a few nanograms per liter³. The term micropollutants (M.P.s) are those, which were previously not considered nor had no significance in the quality of both ground and surface water by distribution and concentration⁴. These compounds were previously not available but are found widely in the recent past and can cause known or suspected adverse effects on human health and ecology. These compounds include natural and synthetic, such as pharmaceuticals and personal care products (PCPs), detergent, steroids, hormones, industrial compounds, pesticides, nanoparticles, and many other contaminants, increasing the environmental concern⁵⁻¹⁶. Bacteria with Antibiotic-resistant genes are also considered as emerging pollutants¹⁷.

Micro pollutants are called 'emerging' because they were not considered and were not included in monitoring programs as their fate, eco-toxicological behaviors are unknown¹⁸. However, it is a challenge to understand EMPs as less information is available. These EMPs started to be detected after the development of sophisticated chromatographic and mass spectrometric techniques¹⁹ at the traces levels, which led to large numbers of research to identify, quantify and catalog the EMPs by publishing them²⁰⁻²⁴.

EMP regulation in various countries

There is a large gap of scientific data relevant to the impacts and fates of EMPs with different concentrations. This has become a hurdle to various Governments around the world to control their usage and handling. It is a matter of more significant concern to handle the EMPs which have already entered the aquatic ecosystem. Specific laws concerning EMPs have not been framed globally, which would mandate concentration limits in any water source treatment plants or nature. The USA prepared an archive of observation techniques to handle enzyme-disrupting compounds and reduce their contact with human or animal life. This document did not have any permissible limits of these compounds in the water but reduced the concentration in consumer products²⁵. The European commis-

sion in 2000 framed a water framework Directive to achieve the good qualitative and quantitative status of all water bodies in the European Union (E.U.)²⁶. In 2013, it released a directive to list 45 priority compounds for their quality in the aquatic environment. In 2015, it added 10 more compounds to the watch list to assess the water quality²⁶.

The E.U. set the permissible limit from 10 ppm and 10mg/kg in surface water and soil to pharmaceutical drugs in the drinking water. In 1998 USFDA gave detailed protocols to assess human drugs, which led to the preparation of an environmental report on each compound and restricted their expected introduction to aquatic environments to 1 ppb²⁷. Switzerland proposed a similar mechanism to European Union's Environmental Quality standards (EQS) for water quality criteria for pharmaceutical compounds and pesticides²⁸. These regulatory bodies of E.U. & USA have tabulated the disinfection byproducts transformed from EMPs and published for general awareness²⁹. But India has no such mechanisms to identify or regulate EMPs³⁰.

In the case of pesticides, every country has its pesticide regulations regarding production, distribution, and utilization. In most countries, their occurrence in drinking water is not regulated through laws even though there are risks to human life and ecology^{31,32}. In the case of India, these are considered as pollutants under the Water (Prevention & Control of Pollution) Act 1974, but their transformed byproducts are not included as pollutants. European Union in 1998 specified the maximum permissible limit of pesticide & their byproduct in water is 1ppb and 0.5 ppb, respectively³³. No specified pesticide was mentioned in this directive but created a monitoring authority to determine the pesticides present in drinking water. This led to identifying several pesticide risk indicators and developing various methodologies with different parameters, including the toxicity of aquatic organisms, assessment of health risks to humans on contact both by occupational exposure and by contaminated water or food³⁴⁻³⁸.

The Environmental Protection Agency (EPA) is an independent body in the USA that takes care of air, water, and soil problems. This agency has evolved over a century along with

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regulations related to the environment. EPA started to look into the adversity of M.P.s in 1985 by preparing detailed guidelines for national water and protecting aquatic life^{38,39}.

Various researches showed the endocrine-disrupting activities by EMPs; EPA published a White paper in 2008. This includes the effect of chemicals on aquatic life during various stages of growth, toxicity, and specific mode of action. This white paper on aquatic life criteria for emerging contaminants was developed to modify the 1985 guidelines^{40,41}.

Japan is a developed country with many water pollution episodes, such as mercury poisoning, cadmium poisoning, organic pollutants in ports, and nuclear pollution. But it has managed to overcome these problems by well-planned regulations and stringent action⁴². The umbrella act, Basic law of environmental pollution control, was enacted in 1967, which concerned human health, control of pollution, and conservation of natural resources. In 1970, a water pollution control law was enacted to protect water resources and was amended in 1995. By mode of follow approach and tightened regulations have given fruitful results^{42,43}.

In this work, we tried to identify some significant chemicals used in various fields, EMPs in the Indian case scenario. Our focus was on chemicals used for crop protection, pharmaceutical drugs and personal care products. Here we tried to quantify them based on their availability to the public and identified their derivatives. In most cases, chemical derivatives were not identified not because of their ability to degrade but because of their insignificant amount in the water sources.

Sources and Movement of EMPs in Environment

When Non-Pathogenic, hazardous material is exposed to humans can cause a significant health risk. This effect increases if these compounds enter into the aquatic source from which drinking water is obtained. In many cases, these EMPs have been seen in drinking water; hence, an attempt is made to identify the pathways. These EMPs all transported through the general model as

1. Source: Agricultural land or Industrial outlet, effluent or Sewage sludge in open land.
2. Flow of EMPs: Through fractures of aquifers, Run-off from Rain Water.
3. The receiver: Crops or tap water for drinking.

Sources of EMPs include wastewater derived from domestic, industrial, hospital premises and waste disposal sites widespread with various openings to the aqueous sources like surface or ground water sediments including pesticides from the agricultural farm, horticultural gardens parks (Figure 1), golf course, urban infrastructure and transport systems, discharge from hospital and industrial waste water which contains various pharmaceutical and PCPs (Figure 2 and 3)⁴⁴⁻⁴⁶. Other sources include sewage and industrial sludge application on land, treatment of animals and pets with pesticides and pharmaceuticals⁴⁷.

Potential sources of E.P.s are Agricultural farms includes crop protection compounds like pesticides, pheromones, hormones sprayed to the crops to protect the harvest. These compounds are deposited on either leaves or soil, leached into groundwater during raining or watering the crops⁴⁸. Thus, a large number of pesticides and their derivatives enter into groundwater or run-off.

Hospital and industrial waste disposal sites in urban areas

are also considered as the sources of EMPs. Polychlorinated biphenyls (PCB), polyaromatic hydrocarbons, alkyl phenols, dioxins furans have been identified in waste water for a long time. Many studies are conducted on waste water treatment effluents, sewage septic tanks, and artificial recharge treated effluents. These waters possess EMPs, majorly pharmaceutical from human excreta and unused pharmaceutical products, rare earth minerals, heavy metals, and contrast Medias⁴⁹⁻⁵⁴.

In many parts of Asia, Europe, and the USA, animals are fed with a concentrated antibiotic diet, an essential source of environmental contamination with EMPs. These antibiotics are seen in waste lagoons, groundwater below lagoons, surface water such as ponds and rivers where this livestock is pastured, and the areas where animal waste is applied to fields as manure⁵⁵⁻⁶¹.

In urban landfills have been a source of polluting ground water. The leachate from the landfill reaches ground water, including caffeine, nicotine, phenols, sterols, and phthalates⁶¹⁻⁶³. Industrial pollutants are also found, such as detergents, antioxidants, plasticizers, fire retardants, and personal care products like antibiotics, anti-inflammatory, and barbiturates⁶⁴.

The path of EMPs in the transmission stage from source to receptors is always unclear. Various factors are involved during the transmission, such as aquatic environment, pH, the solubility of compounds in water, biotic components in an aqueous ecosystem^{65,66}. Considering these factors, the injection of EMPs to groundwater and surface water is studied. EMPs may enter through sewage leakages from septic tanks, wastewater application to agricultural fields, and leachate from landfills. These enter into ground water bypassing the soil zone⁶⁷.

In many cases, treated effluents from sewage and industries are discharged to surface water. The groundwater and surface water interaction is another method of transmission where the difference in density of waters leads to the exchange of compounds. Atmospheric transmission is also a possible case of nonvolatile dust compounds, especially in veterinary and agriculture⁶⁸.

The end-user of water is humans for drinking and farming purposes. In the world, 11% of the population does not have a water supply, and 25% do not have proper sanitation facilities⁶⁹. Hence every government agency utilizes the water available in the area without looking at the quality. Household connectivity of water and public standpipe bore well facilities are provided to improve the drinking water problem and sanitation. Hence the risk of exposure to pollutants is very high. So to reduce the risk, the drinking water treatment is carried out, but the effectiveness of the treatment is significantly less since the concentration is very less can escape from the detectors or indicators⁷⁰.

Wastewaters from animal shelters and agriculture are directly utilized for agriculture, where chemical compounds such as solvents, pesticides, and hormones are uptaken by crop plants and lead to poisoning. This issue has become a global concern as most food items are grown or processed in this water source and transmit the EMPs to far ends of the world^{71,72}.

Not just water and soil, even emerging pollutants in the air have gained attention recently. It is very well-acknowledged in recent reviews that study on micropollutants in the air is marginally studied.

It is known that the primary source of air pollution is the activities happening on soil and water through anthropogenic activities. Having said that, there exist natural sources of pollution such as dust and emissions from wildfires and volcanoes. In totality, particulate matter accompanied by volatile organic

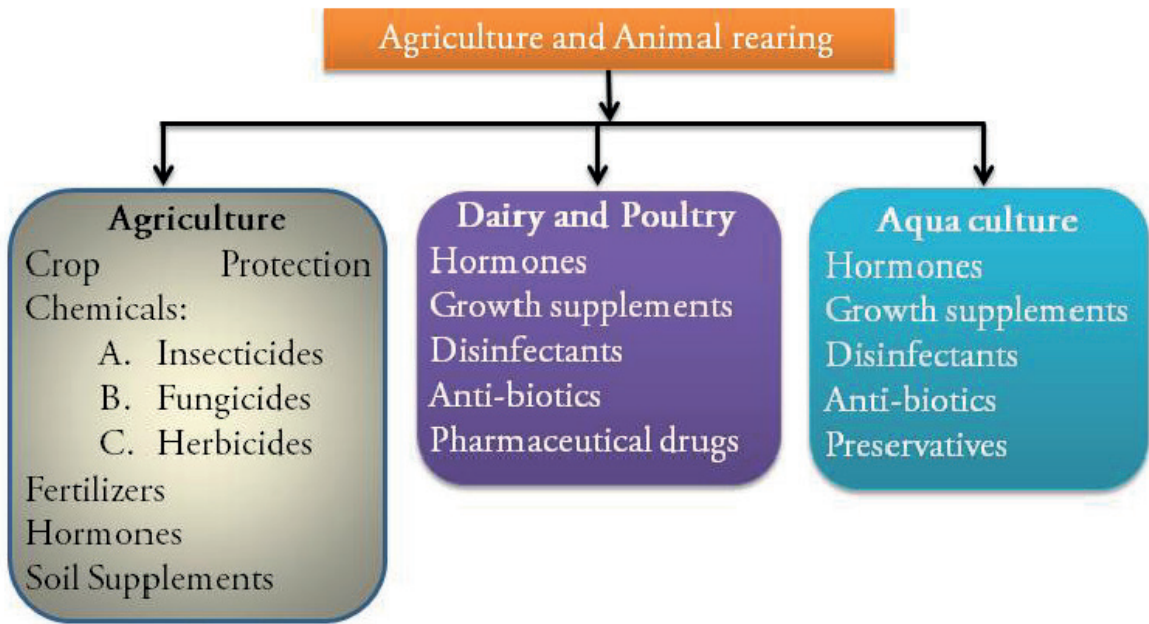


Figure 1. EMPs from Agricultural and allied Source.

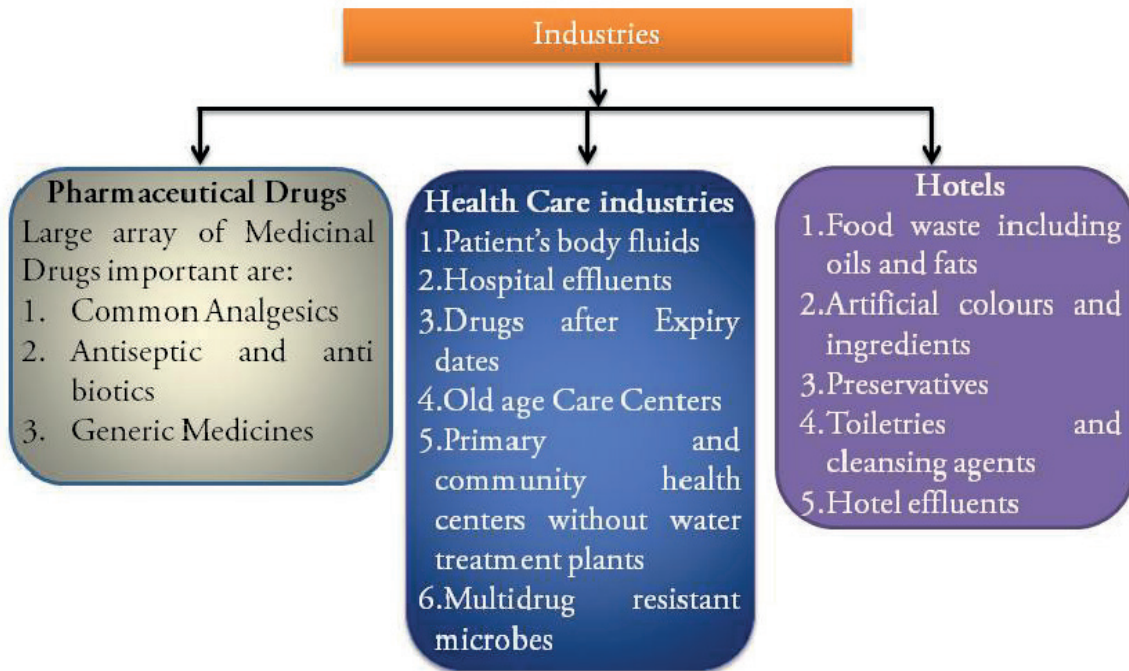


Figure 2. EMPs from various industrial sources.

compounds (VOCs), and other gases form the emerging pollutants in the air⁷³.

Effects of EMPs on different organisms

Hazardous materials are more toxic in lower concentrations and can cause acute and chronic disorders depending on the exposure. EMPs have nanoparticles, antibiotics, endocrine disrupting substances, pesticide derivatives, and hormones that can impact the organisms' daily activities and internal biology. The effects may be invisible in the initial stages, but continuous exposure can cause severe cellular imbalance. The list of EMPs and their adverse effects are tabulated in Table 1.

Crop Protection chemicals

Indian sub-continent has extended from equatorial to sub

tropical regions 8° N to 38° N and spread through 70° E to 98° E. It has compressed every ecosystem. Tropical Region is the primary structure of India, so the condition is favorable to grow the majority of crops and fruits. Hence, agriculture is the principal occupation that contributes 18% to the GDP of the Indian economy. Approximately 58% of the Indian population depends on agriculture for their daily livelihood. Export of cotton and production of sugar is expected to be increased by 9% and 23% by the end of 2018. India is the second-largest producer of fruits and the largest producer of spices globally⁸⁵.

Crops are exposed to various pests, and to protect them from loss, hundreds of pesticides are produced and imported. Pesticides are of various types in the market depending upon the mode target-based and molecule-based. These are broadly classified into insecticides (Action on insects, mainly

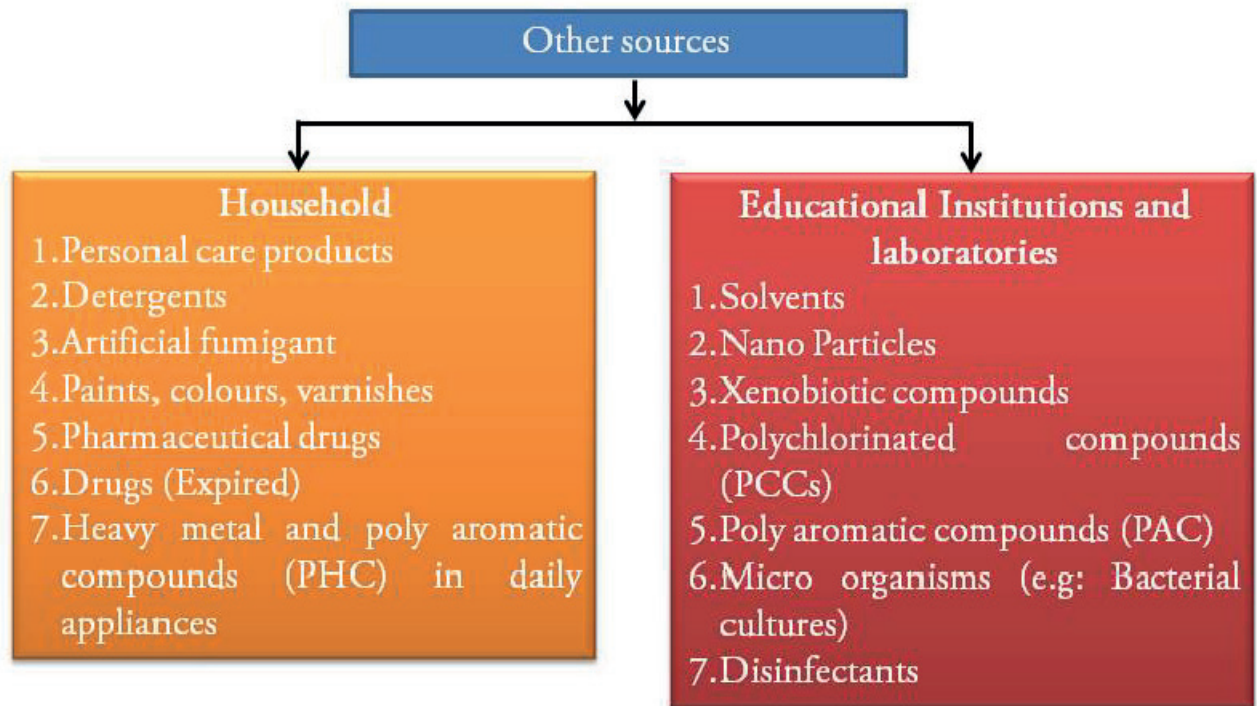


Figure 3. EMPs present in sewage and other wastewaters

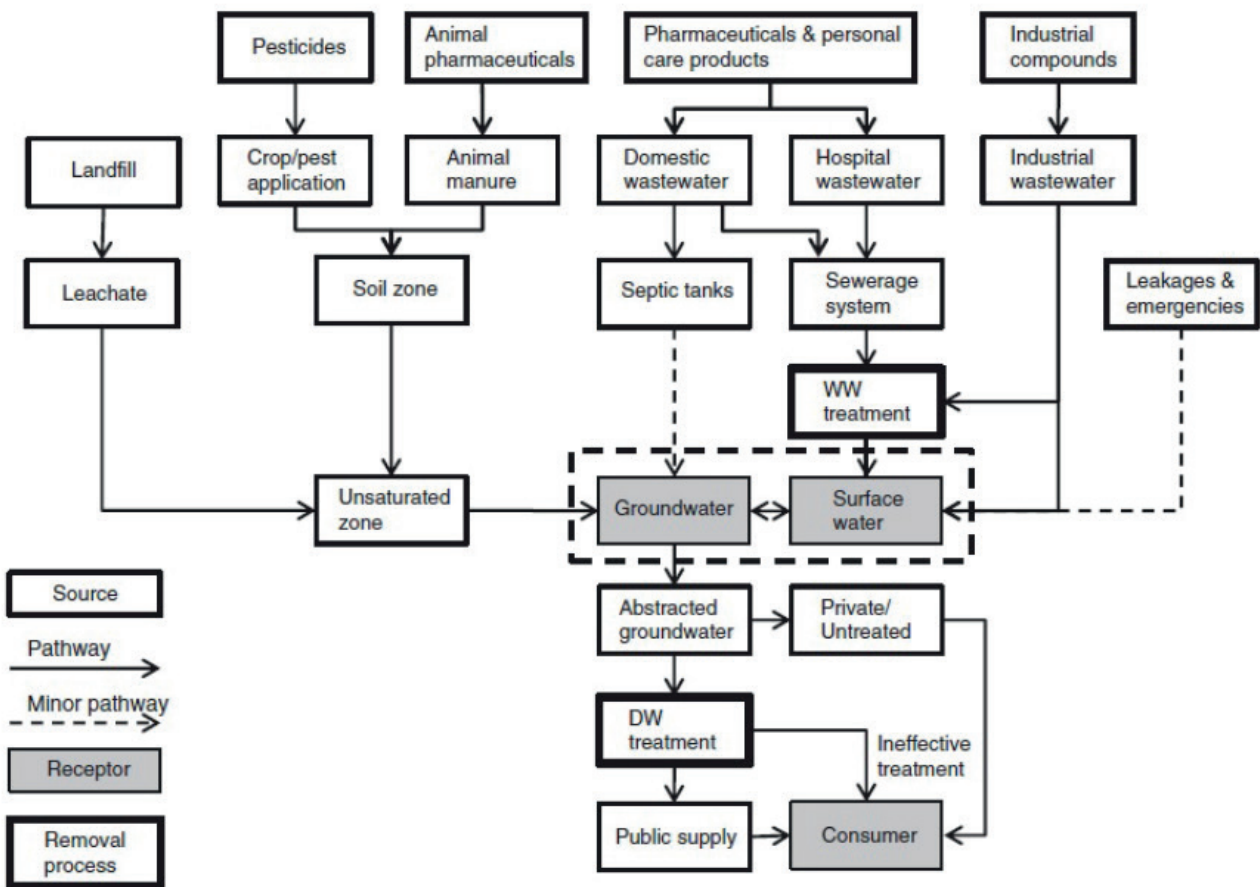


Figure 4. Expected pathway of EMPs from source to receiver.

Compounds	Adverse effects	References
Penicillin, sulfonamides, tetracyclines (Antibiotics)	Resistance among bacterial pathogens that leading to antibiotic-resistant strains, reduction of efficiency of treatment plants by reducing the microbial number	74,75
Caffeine (Stimulant)	Endocrine disruption of goldfish (<i>Carassius auratus</i>)	76
Diclofenac (Nonsteroidal anti-inflammatory drug)	Renal lesions and gill alterations of rainbow trout (<i>Oncorhynchus mykiss</i>)	77
Triclocarban (Antimicrobial agents)	Growth inhibition of algae (<i>Pseudokirchneriella subcapitata</i>)	78
Bisphenol A (BPA) (Endocrine-disrupting compound)	Show estrogenic effect and hormonal disruption leads to increase in risk of breast cancer in humans	79,80
Estrone and 17-β estradiol (steroidal estrogens) and 17-α ethynylestradiol (synthetic contraceptive) – contained in contraceptive pills	Causes change of sex in fishes (feminization), mimics estrogen hormone	69,77
Preservatives, i.e., parabens (alkyl-p hydroxybenzoate) – used for anti-microbiological preservatives in cosmetics, toiletries, and even foods	Mimic Estrogenic Activity	77,81
Disinfectants/antiseptics, i.e., (triclosan – used in toothpaste, hand soaps, acne cream)	Reduction of the number of microbial in treatment plants by acting as biocides agent.	82,83
Benzalkonium Chloride (Disinfectant)	The observed increase in antibiotic resistance	84

Table 1. List of EMPs and Adverse effects.

arthropods), fungicides (activity on the unwanted and harmful fungi species), and herbicides (action of unwanted herbs and bushes). Other categories include rodenticides (mammals like rats, mice, and bats) and bactericides. The pesticides used in India over the year 2012 have been shown in figure 5⁸⁶.

Pesticide usage pattern in India

Currently, India supports 18% of the world population within 2.4% of the land and 4% of the water resources. India planned a green revolution to feed the enormous population and had successes. Indian Agriculture depends on Monsoon rains. Hence, the requirement to procure and maintain stock happens during pre-monsoon and post-monsoon seasons⁸⁸. The requirements of pesticides are regularly checked during a zonal conference on the information of Karif and rabi by individual states. The Government of India will store these pesticide data to plan its agriculture policies for the next financial years. In the figure, 6 data of overall pesticides consumption and consumption per hectare are given from 1992-1993 to 2012-2013. The figure shows that the consumption of pesticides has declined from 72,130 tonnes to 56,090 tonnes. In 2015-2016 and 2016-2017, the consumption of pesticides was 53,719

and 56,215 tonnes, respectively. The consumption of pesticides has been fluctuating because of rainfall, pest infestation, and market availability. The main reason for the reduced use of pesticides is the awareness given by the states for their hazardous nature, and the importance of organic farming has yielded favorable results. And the development of new generation products that have shown to be highly effective at lower quantities is also a reason for the lower use of pesticides⁸⁷⁻⁸⁹.

Though the loss of crops due to pest attacks is high in India that is 15-25% of the produced is lost, the intensity of pesticides consumption is significantly less than 600 g/ha. This number has varied through the years. It has not crossed 1kg/ha. This fluctuation from the year 1992-1993 to 2012-2013 has been shown in the figure. The other countries with high intensity of pesticides consumption are China (14 kg/ha), Japan (11kg/ha), and the USA (4.5 kg/ha), and the world average is 3kg/ha. Indian share of pesticides is about 3% of overall production, used for 16.4 million hectares under cultivation (9% of the total land)⁸⁶.

State-wise use of Pesticides

The variations of pesticides consumption in different sta-

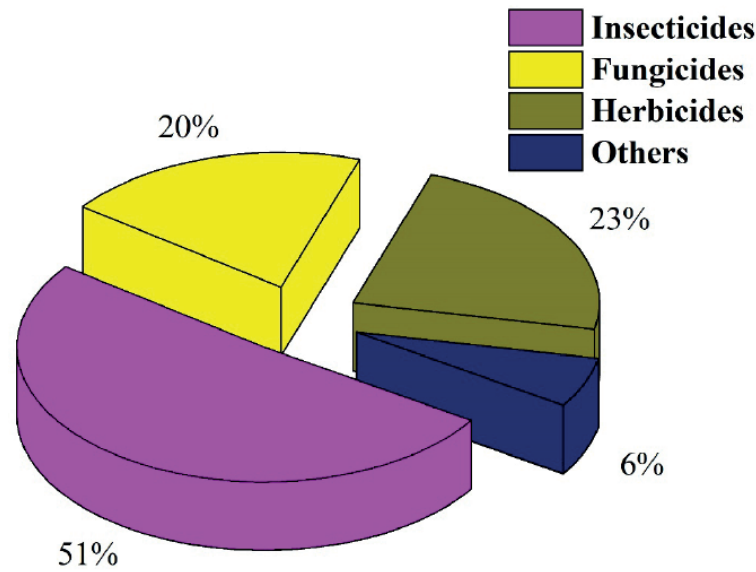


Figure 5. Overall Share of Pesticides Consumed in 2012⁸⁷.

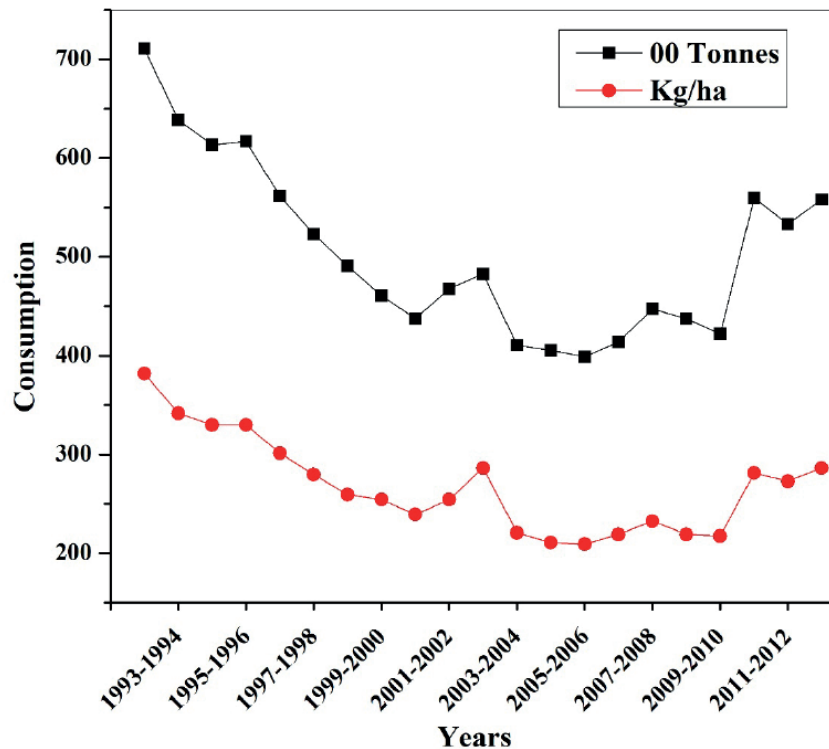


Figure 6. Consumption of pesticides in India (Black overall consumption and red the intensity of consumption)^{87,90}.

tes are shown in figure 7. Maharashtra, Uttar Pradesh, and Punjab are consuming higher pesticides with 13,500 tonnes, 10,200 tonnes, and 5,842 tonnes, respectively. These areas of Uttar Pradesh, Punjab, Haryana are in the plain of perennial rivers; hence annual crops are grown in turn requiring pesticides year long. Maharashtra is a state of cash crops and horticultural crops which require pesticides regularly. The states of South India utilize fewer pesticides due to organic farming that have been popularized in these states. In Kerala and a few parts of Karnataka, the victims of endosulfan pesticides are residing. Assam is the only state using many pesticides where Paddy is grown⁹⁰. Both acute and chronic poisoning of endosulfans in humans is reported extensively. The reports majorly

suggest the toxicity and harmful effects of endosulfans in Kasargod.

Crops and pesticides

The agricultural field has many single species of crops (Monoculture), increasing the chances of damage. Cash Crops are fruits, vegetables, cotton, plantation crops like coffee, tea, ginger etc., where a significant amount of crop protection chemicals are used. India is a tropical country and is exposed to a vivid type of climate which facilitates the parasites to easily infect and transmit to the whole crop field in no time. Thus, large numbers of these chemicals are put to the field where a part controls the pest, but the remaining part is leached out

to soil or water. In figure 8, the number of pesticides used in various crops is mentioned. About 50 % of the pesticides are used on cotton because on every 15-day cycle; the pesticides are applied to kill and control large numbers of pests such as American bollworm, tobacco caterpillar, jassids etc. About 18% of crop protection chemicals are used on paddy fields. Paddy fields are exposed to insects such as plant hopper, rice bug, stem borer, fungal infections such as root and stem rots etc., and other pests include snails and birds mice, which are potent in reducing the production of crops.

Following paddy, crops of fruit and vegetables are primarily exposed to pests. In the preliminary stages, they include bacterial and fungal infections. During the fruiting season, insects, rodents, and mammals such as squirrels and bats attack the plantation. These are also exposed to a variety of weeds since these plantations are sparsely cultivated. Thus large quantities of chemical compounds are sprayed to the plantations to overcome this menace.

Following them, plantation crops (8%) and cereals and millets (7%) stand in the line. These plantation crops like coffee and tea are cultivated in elevated areas where rainfall is high, and the cereals and millets are cultivated in a dry land with less water availability where both the conditions will increase the risk of pest infestation; chemical compounds are used⁹⁰.

Top pesticides produced in India

In the table above, 3, Insecticides, fungicides, and herbici-

des produced are listed. Since India is a tropical country, most of the crops are infested with arthropods. Therefore, insecticides are majorly produced in the country compared to herbicides and fungicides. Organo-Phosphate pesticides are increasing in number because they are effective. Their residence time is 6-8 months. This gives the farmer an interval between two sprays.

Top pesticides used in India

Since India is a tropical country, most of the crops are infested with arthropods. Therefore, insecticides are majorly produced in the country compared to herbicides and fungicides. Previously Organo-chlorides dominated the pesticide field due to their effectiveness and persistence for longer durations. These were banned after various researches showed the cause of cancer and other endocrine disruption activity. Recently organo-Phosphate pesticides are being replaced, and residence time is hardly 6 months. This gives the farmer an interval between two sprays. In figure 9, major insecticides, fungicides, and herbicides produced in India in 2016 are given.

Comparison of Pesticide Regulation in India with the developed country

According to the Insecticide act 1968, more Chemical formulations and 110 combinations of crop protection chemicals have been registered. This act looked into the registration, manufacture, and distribution of pesticides⁹². Under this act, Central Insecticide Board and Registration Authority (CIBRA)

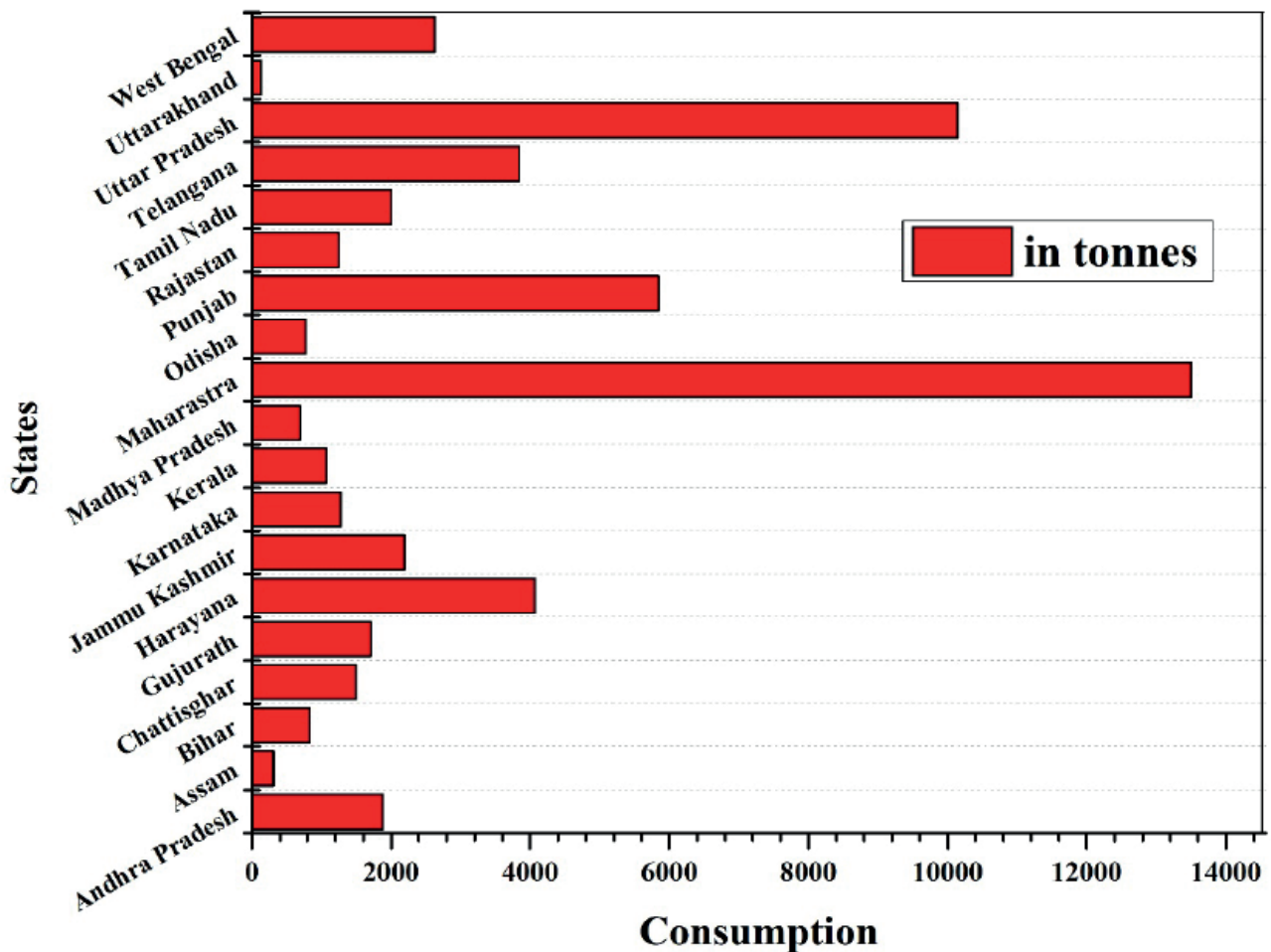


Figure 7. State-wise consumption of pesticides in the year 2016-17^{88,91}

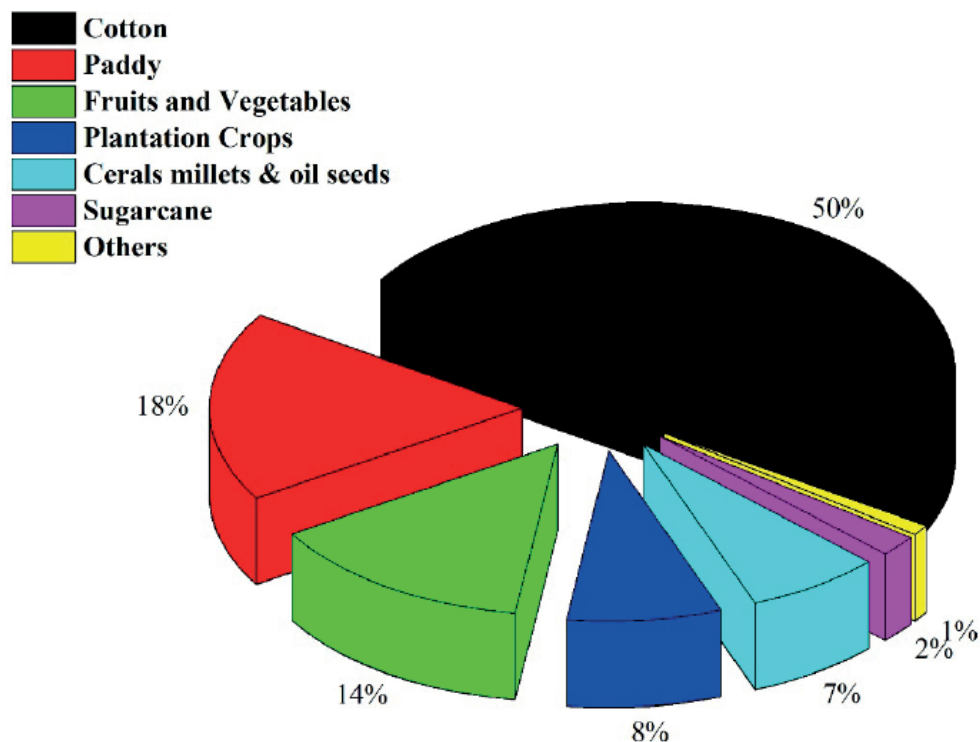


Figure 8. Percentage of Pesticides used on different crops⁸⁶.

Crop Protection Chemicals	Type	Mode of Action	Volume of Production (in Metric tons)	Residues Expected
Cartap	Carbamate	Insecticide	50000	4-(N,N-dimethylamino)-1,2-dithiolane
Acephate	Organo-phosphate		20000	Methamidophos
Chlorpyrifos	Organo-phosphate		10000	3,5,6-Trichloro-2-Pyridinol
Clodinfop	pyridyl phenyl ethers	Herbicide	10000	Persistent
Glyphosate	Organo-phosphate		8000	Aminomethylphosphonic acid
Pretilachlor	Chloroacetamide		5000	2-chloro-N-(2,6-dimethylphenyl)-acetamide
Mancozeb	Dithiocarbamate	Fungicide	6000	Ethylenethiourea (ETU)
Copper Oxchloride	Metallic		4000	copper oxalate
Hexaconazole	-		4000	1,2,4-Triazole, 1H-1,2,4-Triazol-1-yl acetic acid

Table 2. Top 3 insecticides, herbicides, and fungicides produced in India along with the ir residual derivatives in water^{86,90,91}.

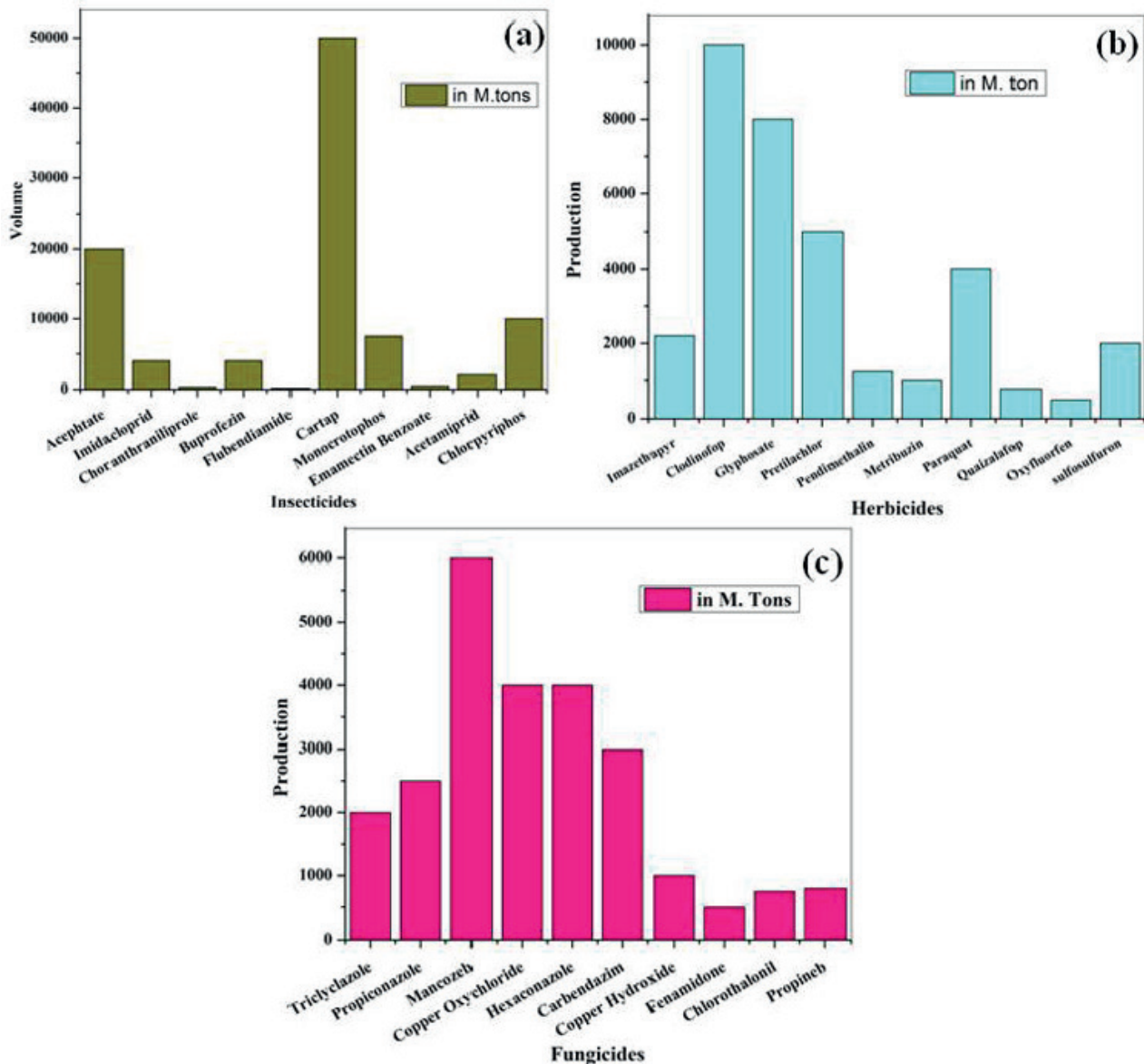


Figure 9. Different pesticides produced in India in 2016 (a. Insecticide, b. Herbicide, c. fungicide).

was set up, which carried out pesticide registration, evaluation related to the product chemistry, bio-efficacy, and toxicity. This regulatory body has banned 70 pesticides from importing and exporting or manufacturing in India^{93,94}.

In 2006, the Food Safety and Security Authority of India (FSSAI) was formed under Food Safety and Security Act to look into the quality of food material. Under this act maximum, residual limits of pesticides were set. To strengthen the law on insecticide, in 2008, a new regulation pesticide management bill was introduced to limit tolerance limits to pesticides according to the Food Safety and Security Act^{89,95,96}.

European Union

European Union has been straightening regulations regarding pesticides and plant protection chemicals. They have been evolving over the years with the current thematic strategy for pesticides. The European Union's health and Consumer Protection Directorate-General (under European Commission) is the regulatory body responsible for looking after the matter related to food health, pesticides and the member states authorize the use or ban of the products in their territories.

The lowest analytical permissible value of pesticides is set to 0.01mg/kg. The E.U. rules do not specify the pesticide or the crop in which they are used. A detailed protocol for sampling and determination of pesticide residue concerning maximum residual level is given in SANCO/12571/2013^{97,98}.

USA

In the USA, the United States Environmental Protection Agency is in-charge of pesticide registration and regulation. USEPA establishes the permissible risk limits of pesticide exposure, both occasional and occupation and child health on exposure. In most cases, tolerance exemptions are not allowed and are maintained consistently. Other Agency U.S. Department of Agriculture handles the pesticide detection in Agricultural products, meat, and poultry eggs. USFDA takes care of food material produced and imported into the country where it checks for the detection of pesticide and restricts the product to enter^{97,99-103}.

Japan

Japan is the largest consumer of pesticides in the world.

The regulatory body is the Ministry of Health, Labors, and Welfare. Japanese laws were general on food safety regarding poisonous and determined substances and did not specify any pesticides. In 2003, the pesticide limit was approved with a positive list. Under food sanitation law in 2006, maximum residue limits of pesticides were set under a positive list system. After the implementation, all agricultural products and imported products had to follow the procedures as per the positive list system. The highest tolerance limit was set to 0.01 ppm^{42,43,104,105}.

Pesticides found in Indian Waters

At the source, near the agricultural field, their concentration is very high. When the water enters the stream, these compounds dilute, thus reducing the chance of detection, which cannot be treatable. These untreatable, untraceable species cause emerging pollution in drinking water. In Tables 3 and 4, a list of pesticides found in groundwater and surface water in India is given.

Pharmaceutical drugs

Pharmaceutical drugs are the compounds used as medicines in the cure of illness. These come in various types and forms, such as tablets, syrups, injection solutions, powder, inhalers. Illness may be to the man or animal; these are considered as lifesavers. These pharmaceuticals are used broadly and progressively are leading to ecological contamination. Broad-spectrum Antibiotics, legal and illicit drugs, analgesics, steroids, beta-blockers, and others are causing environmental issues¹⁰⁷⁻¹¹⁰. Pharmaceutical pollutants are creating secondary pollutants called antibiotic-resistant microorganisms, which are also the reason for concern. The Active pharmaceutical ingredient (API) and their biotransformation are least studied, are the reason which nobody can anticipate their consequences to the ecosystem¹¹¹⁻¹¹³. These compounds have entered the ecosystem in the past 100 years, but the study on their adverse effects started recently¹¹⁴.

Pharmaceutical drugs were not previously considered pollutants as they were entering the environment in lower concentrations; hence, they were considered pseudo pollutants. Over 160 pharmaceutical drugs are being detected in the water at lower concentrations of ng/L to ppm. Hence their eco-toxicological analysis and impact studies are inadequate to handle them^{112,115}.

In table 5 list of top 20 drugs prescribed in India which includes both generic and bulk drugs. In India, the highest prescribed drugs for lifestyle disease, specifically diabetes, then paracetamol, antibiotics, analgesics, and antiallergic drugs are followed by them¹¹⁶.

In the case of the USA, the condition is different. Paracetamol is a highly prescribed drug followed by Anti hypertension, antacids, antibiotics, and antidiabetics¹¹⁷. We could not find the number of drugs prescribed, but their revenue generated was identified.

India and Pharmaceutical Industry

Indian has a well-established pharmaceutical and healthcare industry. India is the third-largest pharmaceutical supplier, and about 40% of these drugs are generic. Pharmaceutical industries have been developed such that India supplies about 50% of global vaccines. India supplies 80% of the anti-retroviral drugs used for combat acquired immune deficiency syndrome (AIDS).

The Healthcare industry is well spread in India with hospitals, telemedicine, medical tourism, health-related finance

solutions. Both the Government and private health care delivery systems are operational. As of 2015, more than 1.8 lakhs hospitals are operational in India, including government hospitals, private nursing homes, primary and community health care centers (PHCs and CHCs)^{8,17,118,119}.

Along with these credits, India is also the world's most significant consumer of Antibiotics. Carbapenem, a lifesaving antibiotic drug available, is sold on a large scale without prescription. Reports related to illicit prescription drugs are used for narcotics drugs leads to illegal production houses and dumping.

EMPs generated by pharmaceutical industries and hospitals are detected in the Indian environmental samples at higher concentrations. Waters and sediments of Hyderabad have turned into poisons because of pharmaceutical wastes dumped into nearby water bodies and landfills¹²⁰⁻¹²⁴.

Detection of Pharmaceutical drugs in various regions

Northern states

Pharmaceutical drugs have been recorded in various water sources. The river Ganga (Haridwar, Kanpur, Allahabad), Yamuna, and at specific points of groundwater (Uttarakashi, Varanasi, Bhagamarg), wastewater (Kanpur, Ghaziabad, Delhi) STPs and secondary sludge (Delhi, Haridwar), sediment and drinking water (Gomathi river and Delhi), these EMPs were detected. Reports show that traces of drugs like caffeine, ibuprofen, paracetamol are found in River Ganga and Yamuna, along with higher concentrations of amoxicillin (Nondetectable levels to 172.6 ng/L).

Antibiotics such as amoxicillin, Ciprofloxacin, gatifloxacin are detected in STP effluents in Delhi. Anti-inflammatory drugs like ibuprofen, diclofenac, antiepileptic drugs (carbamazepine), and other drugs were found in various samples at Ghaziabad and Lucknow in Uttar Pradesh. At SAS Nagar in Punjab, groundwater is contaminated with diclofenac¹²⁵⁻¹³¹.

Southern states in India

These states are highly polluted with pharmaceutical wastes. The study starts at Patancheru near Hyderabad, turns out to be a point source of APIs. This area has a vast number of pharmaceutical manufacturing situated here made an important center for bulk drug production. High concentrations of APIs were found around the effluent treatment plant, of which 21 APIs are above 1ppm Ciprofloxacin, an antibiotic, was detected with the highest concentrations (31ppm), which is higher than the maximum therapeutic human plasma level. It was found even in sediment, surface, ground, and drinking water around 3 km. The effluent is released into Musi River, and the concentration of Ciprofloxacin is 35.4 - 6058 µg/L in water and 11.4 - 4763.3 ng/l in sediments. Other than antibiotics, antifungal agents, fluconazole was found in the sewage of nearby areas. The famous Hussain Sagar Lake of Hyderabad has norfloxacin, and sulfamethoxazole was found^{53,124,125,128,132-136}.

Other categories of pharmaceutical drugs are detected in South India, such as Udupi, Bangalore, Coimbatore, Chennai landfills. It is reported that 5.1kg of caffeine and 2.1kg ibuprofen are discharged annually to SIP in Udupi¹³⁷⁻¹³⁹.

Eastern and western zones

Few reports found in these regions, indicating gaps in pharmaceutical pollution research in these areas. Most illicit drugs and pharmaceuticals are found in the surface waters of Saidpur and Bener in Bihar. Ibuprofen and amphetamine were

Place	Pesticide	Pesticide detected	Quantification technique
Jaipur, Rajasthan	Heptachlor epoxide,	0.943 mg/kg	GC-ECD
	Heptachlor,	0.736 mg/kg	
	Aldrin	0.336 mg/kg	
Dug wells, Unnao, UP	ΣAldrin	BDL-1355.2 ng/l	GC-ECD and GC-MS
	ΣChlordane	BDL-7.2 ng/l	
	ΣEndosulfan	BDL- 54.4 ng/l	
	ΣDDT	BDL-266 ng/l	
	ΣHCH	0.56-2920.9 ng/l	
	ΣHeptachlor	BDL-303.6 ng/l	
	Hyderabad, A.P.	Lindane	
DDT		0.15-0.19 ppb	
α Endosulfan		1.98-2.86 ppb	
β Endosulfan		0.30-0.32 ppb	
Hisur, Harayana	ΣHCH	0.41-2.31 ppb	GC ECD and NPD
	ΣDDT	0.05-0.86 ppb	
	ΣEndosulfan	0.02-0.37 ppb	
	Cypermethrin	0.02-0.09 ppb	
	Deltamethrin	0.17-0.06 ppb	
Sonapur Greater Kolkata WB	Aldrin/dieldrin	0.01-0.03 ppb	GLC
	Dicifol	0.02-0.03 ppb	
Nanded, Maharashtra	Endosulfan	1.50-4.00 ppb	GC-ECD
	Heptachlor	0.00-0.03 ppb	
	Aldrin/dieldrin	0.01-0.04 ppb	
	HCB	1.00-2.00 ppb	
	DDT	2.00-4.00 ppb	
Bore wells of Delhi region, Delhi	α-HCH	0.003-0.005 ppb	GC ECD and GC MS
	β-HCH	0.008-0.037 ppb	
	γ-HCH	0.007-0.014 ppb	
	δ-HCH	0.013-0.039 ppb	
	Heptachlor	0.028-0.032 ppb	
	Aldrin	0.011-0.034 ppb	
	α Endosulfan	0.034 ppb	
	Heptachlor epoxide,	0.016-0.026 ppb	
	dieldrin	0.009-0.058 ppb	
	DDE	0.018-0.046 ppb	
	Endrin	0.029-0.054 ppb	
	β Endosulfan	0.031-0.060 ppb	
	DDD	0.024-0.055 ppb	
	Endosulfan Sulfate	0.036-0.057 ppb	
	DDT	0.068-0.093 ppb	
Methoxychlor	0.066-0.094 ppb		

Table 3. Pesticide found in Ground water and their analytical techniques¹⁰⁶.

Lake/River/ Place	Pesticides Detected	Detected concentration	Detection method
Unnao, UP	Aldrin	BDL-1.88 ppb	GC ECD and GC MS
	Σ Chlordane	BDL-0.04 ppb	
	Σ DDT	BDL-0.23 ppb	
	Σ HCH	1.88-1.95 ppb	
	Σ Heptachlor	BDL-0.11 ppb	
	Methoxychlor	2.63-3.72 ppb	
Greater Kolkata, W.B.	Lindane	0.01-0.05 ppb	GLC
	HCH	0.01-9.90 ppb	
	Aldrin/dieldrin	0.01-0.90 ppb	
	Dicofol	0.01-14.03 ppb	
	DDT	0.01-1.40 ppb	
Baratagi lake, Bijapur, Karnataka	Endosulfan	0.00025 mg/kg	GC ECD and GC MS
	Chlorpyrifos ethyl	0.0002 mg/kg	
	4-bromo-2-chlorophenol	0.0003 mg/kg	
Hisar, Haryana	Σ DDT	50.1-332.2 ng/l	GC ECD
	Σ HCH	2.3-560.6 ng/l	
	Σ Endosulfan	BDL-206.3 ng/l	
Khindsi lake, Bhandara, Maharashtra	α-HCH	0.019-0.120 ppb	GC ECD and GC MS
	β-HCH	0.031-0.061 ppb	
Tamiraparani river basin (TN)	Σ HCH	0.01 ng/l	GC MS
	Σ DDT	0.01-0.72 ng/l	
	Heptachlor	0.06-2.1 ng/l	
	Aldrin	0.02-1.5 ng/l	
	Trans-chlordane	0.01 ng/l	
	Cis-chlordane	0.01 ng/l	
	Dieldrin	0.03-7.5 ng/l	
	Endrin	0.02-58.0 ng/l	
	Mirex	0.01-0.47 ng/l	
Rishikesh, Ganga river, Uttarakhand	Σ HCH	5.54 ng/l	GC ECD and GC MS
	Σ DDT	1.01 ng/l	
	Σ Endosulfan	0.92 ng/l	
	Σ Aldrin	1.89 ng/l	
	Σ Heptachlor	0.32 ng/l	
Cauvery river, Karnataka	α-HCH	0.87 ppb	GC ECD
	β-HCH	0.56 ppb	
	γ-HCH	0.93 ppb	
	δ-HCH	0.78 ppb	
	p. p' -DDT	0.64 ppb	
	p. p' -DDE	0.96 ppb	
	p. p' -DDD	0.53 ppb	
	Endosulfan	0.84 ppb	

Table 4. Pesticides residues in Surface water¹⁰⁶.

Sl. No.	Brand Name	Active Pharmaceutical Ingredient (API)	Class of Pharmaceutical	Company	Moving Annual Turnover (in Rs. Cr)
1.	Mixtard	Soluble Insulin	Anti-Diabetic	Novo Nordisk, India	512
2.	Glycomet	Metformin	Anti-Diabetic	USV	415
3.	Spasmo Proxyvon Plus	Dicyclomine, Paracetamol, Tramadol	Anti-Cholinergic and Analgesic	Wockhardt	377
4.	Lantus	Insulin glargine	Anti-Diabetic	Sanofi India	341
5.	Galvus	Metformin-Vildagliptin	Anti-Diabetic	Novartis India	328
6.	Liv52	Natural Ingredients	Hepato Protective	Himalayan Grugs	296
7.	Janumet	Sitagliptin, Metformin	Anti-Diabetic	MSD Pharma	285
8.	Augmentin	Amoxicillin, Clavulanate potassium	Anti-Biotics	GSK	283
9.	Clavam	Amoxicillin, Clavulanic Acid	Anti-Biotics	Alkem Labs	281
10.	Monocef	Ceftriaxone	Anti-Biotics	Aristo Pharma	277
11.	Voveran	Diclofenac	Analgesic and Anti-inflammatory	Novartis India	266
12.	Novomix	Protamine-crystallised Insulin	Anti-Diabetic	Novo Nordisk India	263
13.	Betadine	Povidone-iodine	Antiseptic	Win Medicare	253
14.	PAN	Domperidone, Pantoprazole Sodium Sesquihydrate	Anti-ulcer	Alkem Lab	250
15.	Volini	Diclofenac Diethylammonium Topical, Menthol Topical, Methyl Salicylate Topical, Oleum Lini Topical	Analgesic and Anti-inflammatory	Ranbaxy	248
16.	Synflorix	Pneumococcal Polysaccharide Conjugate	Vaccines	GSK	237

Table 5. Top pharmaceutical drugs produced in India with APIs and category¹⁷.

17.	Phensedyl Cough Linctus	Promethazine, Codeine, Ephedrine	-	Abbott	228
18.	Aciloc	Ranitidine	Anti-ulcer	Cadila Pharma	225
19.	Foracort	Formoterol Fumarate, Budesonide	Anti- Allergic	Cipla	224
20.	Becosules	Multi Vitamin	-	Pfizer India	223

Table 5. Top pharmaceutical drugs produced in India with APIs and category 118

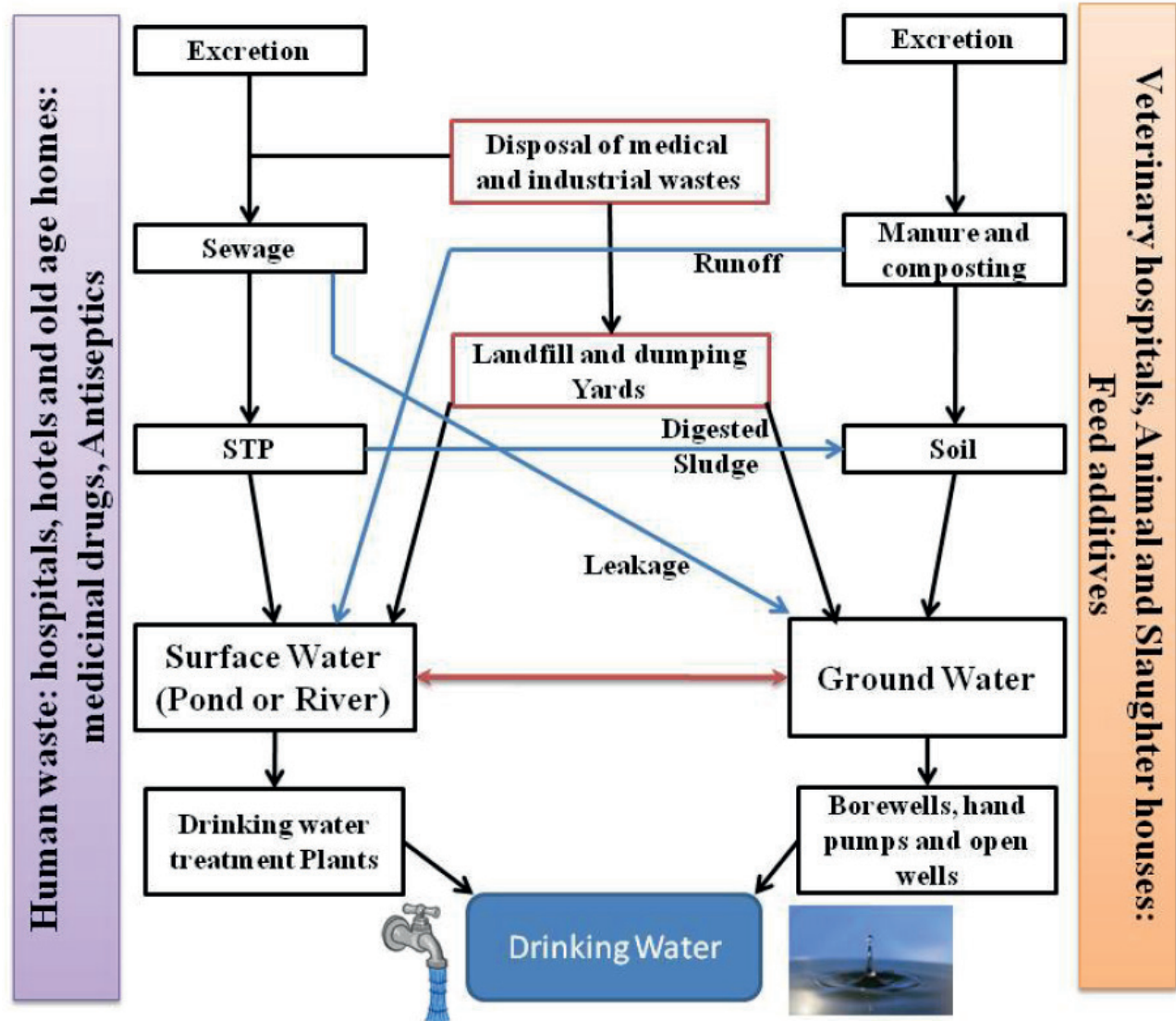


Figure 10. Pathway of transmission of pharmaceutical drugs..

found in the effluent (1130 ng/L) and sludge samples (1230ng/L)¹⁴⁷⁻¹⁴⁹. In western parts of Maharashtra's Nagpur, antibiotics and antidepressants were found in Nag and Pili River. More than 12 APIs are detected in 2 wastewater treatment plants of one of the largest metropolitan areas of western India. The concentration of pharmaceutical drugs varies in treatment plants because of zonal planning, seasonal diseases, medicinal patterns, lifestyle-related disorders, and rainfall^{140,141}.

Antibiotic use in India

India is the largest consumer of antibiotics. From the past decade, 62% of usage has been an increase of antibiotics. In-

dia has consumed 12.6×10^9 units of antibiotics during the past decade, and Per capita antibiotics consumption was 10.7 units¹⁴². The reason is poor public health systems, the high rate of tropical infectious diseases and the availability of antibiotics at cheaper rates. Indian health care system depends on doctors who routinely receive remuneration on prescribing antibiotics, and another reason is that patients are not willing to give time for the disease to cure by the body's innate immunity¹⁴³⁻¹⁴⁶.

Antibiotics in animal husbandry have also resulted in more excellent pathogens because of increased demand for poultry, meat, and related products. According to a report, the

demand for poultry will be raised by 312% by 2030. To cater to that demand, this sector is expected to be investing in Antimicrobial chemical drugs to nearly \$ 1.2billion.

Dairy Industry has developed two-fold in India over the past 2 decades because of the increase in demand for milk and dairy-related products. Milk is considered a complete food because of its protein and fat contents. Nowadays, antibiotics are being used frequently in lactating animals to promote animal health, treatment and control of the infectious disease. Mastitis is a significant disease in dairy animals where the treatment involves antibiotics to mammary glands. Other reasons include using dosage deviations from recommended prescriptions, using antibiotics as preservatives, maintaining incorrect cleaning orders, and veterinary errors¹⁴⁷⁻¹⁴⁹.

Consequences of Excessive use of Antibiotics

Antibiotics are used to cure diseases that are caused by microorganisms, especially bacteria. Bacteria undergo fast mutation to resist the activity of antibiotic medication is called Antibiotic resistance (A.R.) organisms. In some instances, bacteria that resist multiple antibiotics are called multi-drug-resistant (MDR). If bacteria survive in an extensive antimicrobial environment, they are called superbugs or extensive drug-resistant organisms (XDRs). For bacteria with Antibiotic resistance activity, *Staphylococcus aureus*, *Enterococcus* sp., and Multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB) are a few examples¹⁴⁹.

The evolution of antibiotic resistance (A.R.) and expression of AR Gene in nature has led to significant public health problems around the Global¹⁵⁰⁻¹⁵². If the A.R. gene is integrated into a gene transmission element and can spread to non-resistant species, turn them into Antibiotic-resistant organisms (ARO); for this character, these organisms are making their names in emerging pollutants (EMPs) list¹⁵³⁻¹⁵⁵.

This crisis has led to the differential use of anti-microbial drugs in therapeutic and non-therapeutic purposes at clinical and non-clinical settings. Previously researches were focused on the emergence of these bacteria in hospitals and dumping sites of pharmaceutical wastes. From the last 5 years focus of research shifted to the overall environment, which acts as a site for antimicrobial resistance evolutions. Researchers have found the various bacteria with A.R. genes in environmental samples in natural ecosystems such as sediments, soils, ground, surface, marine and drinking water¹⁵⁶⁻¹⁶⁵.

Personal care products (PCPs)

According to E.U. Regulation 1223/2009 (article 2), "cosmetic product means any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odors"¹⁶⁶.

Substances such as pharmaceuticals, personal care and other endocrine-disrupting compounds products enter the environment from different sources such as:

- (i) Effluents from wastewater treatment plants
- (ii) Leakage from septic tanks or landfill sites
- (iii) Surface water run-off

- (iv) Direct discharge into waters.

These species can also be chemically degraded by microorganisms or by U.V. light action¹⁶⁷.

Personal care products can reach the wastewater system through multiple routes. Products such as shampoos, body washes, and toothpaste are directly washed down the drain during and after use. Products like cosmetics and hand lotions can be washed down the drain as well during a routine. The chemicals that can penetrate the body and are then excreted can also enter the wastewater system through toilet¹⁶⁸.

The environmental safety of household products is assessed based on the ecological properties of their many components. Two fundamental issues determine their environmental safety: the environmental fate and potential effects on the environment. The environmental fate of chemical substances depends mainly on the physicochemical properties, such as water solubility, adsorption behavior, and volatility, and on their degradability, which is overwhelmingly affected by microorganisms (biological degradation) present in sewage treatment plants, surface waters, and soils. These fate-relevant properties control the distribution of a chemical in the environmental compartments (water, soil, air) and its final removal by degradation processes.

The second assessment aspect, the potential impact of a chemical on the organisms living in the environmental compartments, also depends on substance-specific properties, i.e., ecotoxicity. Data from standardized tests on representative organisms are required by European chemical legislation¹⁶⁹.

Disinfectants

Triclosan (TCS) and triclocarban (TCC) are diphenyl ethers used as anti-microbials in soaps, deodorants, skin creams, toothpaste and plastics. TCS and TCC are among the top 10 most commonly detected organic wastewater compounds for frequency and concentration. A study monitoring 95 compounds in surface water throughout the United States found TCS to be one of the most frequently detected compounds with surface water concentrations as high as 2.3 ppb TCC has been used in PCPs since 1957 and has been observed in surface water at concentrations up to 6.75 ppb. It is believed that TCC occurs as frequently in WWTP effluent and surface water as TCS; though, until 2004, TCC could not be detected at low levels (ppb). However, TCC has been detected at higher concentrations and more frequently in WWTP effluent and surface water than TCS or M-TCS over the last 10 years. Acute toxicity of TCS and biphenylol has been examined in invertebrates, fish, amphibians, algae, and plants^{170,171}.

Fragrances

The most used fragrances are synthetic musks. Synthetic musks are used in a wide range of products, including deodorants, soaps, and detergents. The most commonly used nitro musks are musk xylene (MX) and musk ketone (M.K.), whereas musk ambrette (M.A.), musk moskene (MM), and musk tibetene (M.T.) are used less frequently. Nitro musks however are slowly being phased out due to their environmental persistence and potential toxicity to aquatic species. Polycyclic musks are currently used in higher quantities than nitro musks with celestolide (ABDI), galaxolide (HHCB) and toxalide (AHTN) used most commonly and traseolide (ATII), phantolide (AHMI), and cashmeran (DPMI) used less often. HHCB and AHTN production alone has been estimated at 1 million pounds per year and has thus been placed on the High Production Volume List

by the USEPA (the United States Environmental Protection Agency). Nitro and polycyclic musks are water-soluble, but high octanol-water coefficients (log Kow = 3.8 for M.K. and 5.4–5.9 for polycyclic musks) indicate high potential for bioaccumulation in aquatic species^{75,170–172}.

Insect repellents

N, N-diethyl-m-toluamide (DEET) is the most common active ingredient in insect repellents and is routinely detected in surface waters. DEET is relatively persistent in the aquatic environment, but unlike many other PCPs (i.e., fragrances and U.V. filters) DEET has a low BCF and is likely not accumulated into aquatic organisms. DEET has been regularly detected in the effluent (95% of analyzed samples) and surface water (65% of all analyzed samples) with median concentrations of approximately 0.2 ppb and 55 ppb, respectively. The only other insect repellent detected in WWTP effluent or surface water is 1,4-dichlorobenzene. 1,4-dichlorobenzene has been detected in surface water (40% of surface water screened), receiving significant inputs of WWTP effluent at concentrations up to 0.28 ppb^{170,173}.

Preservatives

Parabens (alkyl-p-hydroxybenzoates) are antimicrobial preservatives used in cosmetics, toiletries, pharmaceuticals, and food. There are currently seven different types of parabens in use (benzyl, butyl, ethyl, isobutyl, isopropyl, methyl, and propyl). Only a handful of studies have examined paraben concentrations in WWTP and surface water. The most significant concentrations of parabens have been identified in surface water with concentrations ranging from 15 to 400 ppb depending on paraben, whereas effluent had lower concentrations ranging from 50 to 85 ppb¹⁷².

U.V. filters

U.V. filters are used in sunscreen products and cosmetics to protect from U.V. radiation and can be either organic (absorb U.V. radiation, e.g. methyl benzylidene camphor) or inorganic micropigments (reflect U.V. radiation, e.g. ZnO, TiO₂). U.V. filters are well known to bioaccumulate, and recent studies have also indicated the potential for estrogenic activity. In vitro assays using fish, MCF-7 cell lines indicate five UV-A and UV-B sunscreens (BP3, homosalate (HMS), 4MBC, octyl-methoxycinnamate and octyl-dimethyl-PABA) have the potential to cause estrogenic effects¹⁷³.

Additional compounds

Three additional PCPs have been identified in surface water in the U.S. by United States Geologic Survey researchers. The fixative benzophenone was detected most frequently (67.5% of samples in one study), whereas the flavorant menthol was detected at the highest concentrations (1.3 ppb). The other compound detected in the surface water is methyl salicylate (wintergreen flavoring and liniment), although it has only been detected at low concentrations and in a few environmental samples⁷⁵.

Conclusions

Emerging micropollutants are the problems of present living conditions and lifestyle changes of human beings. The EMPs generated from every human activity like agriculture, healthcare, and sanitation which most of them ends them in water through the sewer lines or at water bodies. Fortunately,

the distribution of EMPs through the air is negligible except during the arial dispersions. The detections of these compounds are significantly less or available in smaller quantity makes them harder to regulate.

Pesticides and other crop protection chemicals are used extensively in agricultural practices and gardening, entering the soil and reaching water through run-off. Air dispersion of pesticides are not much into concern as most of them disintegrate due to sunlight and eventually settle on to the soil.

Health care and hygienic products from hospitals or residential areas are directly entering into sewers, like APIs antibiotics or endocrine disrupting substances that show amplified effects even at lower concentrations. These compounds are usually used in an unregulated manner and disposed of without treatment increases the risk of exposure.

Over the few years, nations have been working on identifying and regulating these EMPs. Countries in Europe and the USA are training their human resources and capacities for identifying and handling these pollutants. Developing countries like India are facing the problem of EMPs in various parts and are coming forward to create legislation to reduce the generation of EMPs.

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Received: 22 June 2021

Accepted: 10 August 2021