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STUDY ON REMOVAL EFFICIENCY OF DIFFERENT MICROORGANISMS IN ANTIBIOTIC-PRODUCING PHARMACEUTICAL INDUSTRIES WASTEWATER

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ABSTRACT: Antibiotic yield has been raised by numerous pharmaceutical firms in response to the rising population, the COVID-19 outbreak, and the introduction of several new diseases. Several heavy metals are used in the antibiotics' formulation. The release of antibiotics and heavy metal ions has wreaked havoc on the ecosystem. The issue with heavy metals is that the bulk of them last a long time in the environment and are a leading cause of different types of cancer and other human diseases. On the other hand, experts worldwide are concerned about the presence of antibiotics in the environment, particularly in wastewater, because it leads to the emergence of antibiotic-resistant microorganisms (superbugs) that can cause widespread damage. Bioremediation is a viable approach for treating pharmaceutical industry wastewater with antibiotics and heavy metal ions. Copper, cadmium, nickel, zinc, lead and iron are common heavy metal ions found in wastewater from antibiotic-producing pharmaceutical firms. Along with it, antibiotics like chlortetracycline, oxytetracycline, cefalexin, Sulfamethoxazole, norfloxacin and ciprofloxacin are frequently found in the effluent of pharmaceutical companies. As a result, this review focuses on the characterization and prospective removal capacities of several microbes for antibiotics and heavy metal ions from pharmaceutical industry wastewater. This review has emphasized the importance of scientific enhancement.

INTRODUCTION: The products from pharmaceutical industries are used for several remedial purposes, antibiotics being one of them. Around the world, several tonnes of antibiotics are produced yearly, and wastewater from such industries has marked the presence of antibiotics in them. Certain metal ions used to formulate antibiotics are also found in the wastewater of such industries.

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Hyderabad, India, has lots of pharmaceutical industries. When researchers analyzed the water from nearby villages, they detected the presence of antibiotics in them, which are also sometimes in high concentrations of mg/L. Hence, it can be stated that groundwater and surface water are getting contaminated with antibiotics and heavy metal ions.

Animals and people or any organism using such contaminated waters with antibiotics can form develop antibiotic resistance over the due course of time. The metals, essential or non- essential are proved to be detrimental at concentrations above the normal. (Rasmussen *et al.* 2000) defined metal toxicity as an inherent capacity or the potential of

certain metal to bring detrimental consequences for living organisms [1]. The ability of the metal ions to remain in the atmosphere for long periods of time is hazardous to living organisms such as humans, animals and plants. For an example, "the average half-life of metal ions such as lead is be around ten years once it enters in humans" [2]. Acidic environment followed by surrounding having nutrient deficiency together contributes to more serious metal toxicity [3]. The epidemic of COVID-19, caused due to the spread of the SARS-CoV-2 virus has also resulted in the increase in the consumption of numerous antibiotic formulations around the world. Antibiotic drugs such as ciprofloxacin [4, 5, 6], tetracycline based antibiotic drugs [6], cefalexin [7], sulfamethoxazole [8], norfloxacin [9] were all recommended suggested for treatment of several bacterial co-infections in patients with SARS-CoV-2 infections [10-15]. Therefore, by employing microorganisms, bioremediation efficiently removes pharmaceutical contaminants such as antibiotics and heavy metal ions from the wastewater detected in the contaminated areas. However, it is observed that some microorganisms can only remove the contaminants at very low concentrations, making them less efficient. Therefore, more emphasis must be given to increasing the efficiency of such microorganism in removing antibiotics and the heavy metal ions detected.

Commonly detected metal ions from antibiotic-producing pharmaceutical industries include Nickel (Ni), Copper (Cu), Iron (Fe), Cadmium (Cd), Zinc (Zn), Lead (Pb), *etc.* **Table 1**. Metal ions used in the production of antibiotics are detected in the wastewater. Commonly detected antibiotics in the effluents include Oxytetracycline, Chlortetracycline, Sulfamethoxazole, Cefalexin, Norfloxacin, and Ciprofloxacin **Table 2**. The current time considers them contaminants that need immediate strict attention since they are released into the environment, more precisely into wastewater and then into waters, sometimes completely untreated.

Removal of Heavy Metal Ions by Microorganisms from Effluent of Antibiotic Producing Pharmaceutical Industry: Antibiotics are certain medicines that are used to fight against bacterial infections. There are several pharmaceutical industries producing antibiotic drugs. However, many different metal ions used to produce these antibiotics are discharged along with antibiotics in the wastewater into the environment. Such metal ions and the antibiotics in wastewater can be treated using different microorganisms in different conditions. In a study conducted by (Lalung 2014, Amin 2019) [10, 11], heavy metal ions and antibiotics from the effluents were detected. The commonly detected heavy metal ions in the effluents of such pharmaceutical industries are listed in **Table 1.**

Several bacteria, fungi, and algae have absorbed metal ions from the antibiotic producing pharmaceutical industries. Interactions of metal ions with the cell wall of these microorganisms act as the first step of the entire biosorption process. The specialized cell wall of each category of microorganism, be it fungi or algae or bacteria have all contributed to the biosorption of the heavy metals.

Bacterial Cell Biology that Aids in Metal Ion Uptake: Based on the uptake of gram staining, bacteria can be grouped into gram-positive and gram-negative strains. The cell wall composition of gram-positive differs from gram-negative strains, which have affected the heavy metals uptake by microorganisms positively or negatively. Gram-positive bacteria such as *Bacillus* sp., *Micrococcus* sp., *Streptomyces* sp. have more peptidoglycan in their cell wall (90%) than gram-negative bacteria (10%-20%). The negative charges in the cell wall are associated with the presence of teichoic acids of the gram-positive bacterium. In contrast, in the case of gram-negative bacterium such as *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, presence of teichoic acids together in association with teichuronic acids and lipopolysaccharides all contributed together to the negative charges of the cell wall [2]. Efflux pumps are made of membrane proteins integrated into the membrane for the biosorption of heavy metal ions [1, 6, 12]. However, less metal biosorption capacity of gram-negative bacteria is linked with the presence of lipopolysaccharides and phospholipids [13, 14]. The initial step in metal ion biosorption is metal interactions with functional groups such as hydroxyl, carboxyl, amine, *etc.* [3]. *Bacillus firmus* and *Bacillus cereus* are the gram-positive bacteria

that have the capability of copper biosorption [11, 15]. Because *Bacillus* sp. possesses a basic cell envelope, the exported protein molecules simply need to pass through the cytoplasmic membrane to exit cell [16]. The copper breakdown is 94 % at a temperature of 30^{o}C in *Streptomyces sp.* AB5A by the mechanism of cupric reductase activity for the breakdown of copper from wastewaters. The absorption of various metals has been attributed to exopolysaccharides generated by bacterial cells. *Bacillus subtilis* biosorb iron by producing exopoly saccharides [17].

Algal Cell Biology that Aids in Metal Ion Uptake: Polysaccharides, namely chitin, xylan, mannan, and others, comprise the cell wall in algae. The functional groups serve as metal ion binding sites. Algal cell walls have the same functional groups as bacteria but contain imidazole-additionally [2]. The major mechanism for the uptake of metal ions occurs when the metal binds on the outer cell surface to the functional groups present. Subsequently, it is internalized, as specified for zinc metal ions uptake by *Nostoc muscorum* [18]. Another example, *Chaetoceros calcitrans* being a microalga shows biosorption ability of copper. According to a study conducted by (Pratiwi *et al.* 2019), *Chaetoceros calcitrans* can biosorb copper from wastewater [19]. "The presence of several functional groups on the surface of *Chaetoceros calcitrans* cells, such as carboxylic, hydroxyl, amino, sulphate, sulfhydryl, and phosphate groups, aids in the biosorption of copper ions" [20]. Furthermore, various proteins and polysaccharides on the cell wall surface aids copper adsorption by binding copper to the cell surface. The amount of Cu absorbed by *Chaetoceros calcitrans*, on the other hand, decreases when the concentration of metal ions rises [21]. *Nostoc*sp. can biosorblead and iron [22], *Nostoc muscorum* can biosorb zinc [59] and cadmium [23], from the wastewaters.

Fungal Cell Biology that Helps in Uptake of Metal Ions: Due to the unique composition of cell walls and the presence of functional groups that act as metal binding sites, fungi such as *Aspergillus niger* have proven to be effective for metal ion biosorption, cadmium [24] and nickel [6]. Lipids, polysaccharides (90 %), chitins, mannans, *etc*., make up the cell walls. Carboxyl, phosphate, proteins, chitins and chitosan are the functional groups that serve as metal binding sites in fungi, chitins and chitosan being specific for fungi [16]. The exterior of the cell wall behaves as ligand for binding metal ions, eliminating the inorganic ions [25-27].

TABLE 1: REMOVAL EFFICIENCY OF MICROORGANISMS FOR HEAVY METAL IONS FROM WASTEWATERS OF ANTIBIOTIC-PRODUCING PHARMACEUTICAL INDUSTRY

To be degraded	Name of microorganism	Type of microorganisms	pH	Temp.	Removal efficiency (% or mg/g)
Cu [5, 9, 11, 28, 29]	*Bacillus firmus, Bacillus cereus, Streptomyces* sp. AB5A, *Chaetoceros calcitrans, Stenotrophomonas maltophila*	Bacteria (+) Bacteria (+) Bacteria (+) Algae Bacteria (-)	3.5, 5.5, 7, -, 5	25^{o}C, 25^{o}C, 30^{o}C -, 25^{o}C	74%, 50.32 mg/g, 94%, ND, 0.57mg/g
Zn [5, 25, 30-32]	*Bacillus firmus, Nostoc muscorum, Sargassum* sp. (Brown Algae)	Bacteria (+), Algae, Algae	-, -, 3	-,- 30^{o}C	69.8%, 66%, 15.4mg/g
Cd [1, 5, 13, 33]	*Nostoc muscorum, Pseudomonas aeruginosa, Chaetoceros calcitrans, Aspergillus niger*	Algae, Bacteria (-), Algae, Fungus	-, 8 -, 4.75	-, 42^{o}C -, 25^{o}C	95.4%, 92% ND, 96.98%
Ni [5, 6, 15, 12, 15, 34]	*Aspergillus niger, Micrococcus sp., Fucus vesiculas*	Fungus, Bacteria (+), Algae	6.8-7.2, 5 5	29^{o}C, 30^{o}C-35^{o}C, 25^{o}C	25.05 mg/g, 55%, 0.8 mg/g
Pb [5, 32, 35, 37]	*Chlorella vulgaris, Bacillus cereus* NSPA8, *Nostoc sp.*	Algae, Bacteria (+), Algae	6, -6.5-7	25^{o}C, 37^{o}C 90^{o}C	78%, 98.3% 99.6%
Fe [26, 32, 38, 40]	*Bacillus subtilis, Sargassum sp. (Brown algae), Nostoc* sp.	Bacteria (+), Algae, Algae	-, 3, 6.5-7	-, 30^{o}C, 90^{o}C	ND, 14.6 mg/g, 97.7%

*ND: Not Determined, (+): Gram Positive, (-): Gram Negative.

Removal Efficiency of Microorganism for Antibiotic Pharmaceuticals in Effluents of Antibiotic Producing Pharmaceutical Industries: Antibiotics on the other hand, are nowadays prescribed largely by health professionals around the world. The COVID-19 pandemic has had a negative influence on the world, increasing antibiotic usage while also

increasing antibiotic production. Hence, due to increased demand, the pharmaceutical industries have increased their production capabilities of such drugs; this is indicated by the frequent detection of antibiotics in high concentration in the effluent from such industries. Antibiotics that are freely available in the environment can create antibiotic-resistant bacteria, which can inflict massive destruction around the planet. However, it is still unknown how the presence of other pharmaceuticals along with the antibiotics mentioned below, will affect the microbes' capability to degrade them.

Some of the most regularly identified antibiotics in pharmaceutical industry effluents are listed below, along with the method of their breakdown by microbes:

Oxytetracycline and chlortetracycline breakdown in the similar way. Both antibiotics found in wastewaters were broken down into the same breakdown product. In their study, (Wang *et al.* 2018) used microbial fuel cells to remove oxytetracycline antibiotics from effluents. The fuel cells reactors were split into open-circuit microbial fuel cells and closed circuit microbial fuel cells. *Stenotrophomonas* sp., *Azospirillum* sp., and *Pandoraea* sp. were found in the closed circuit Microbial fuel cell, while *Stenotrophomonas* sp., *Burkholderia* sp., and *Pandoraea* sp. were found in the open circuit Microbial fuel cell. After seven days, it eliminated 78 percent of the oxytetracycline and 74.2% chlortetracycline [41] **Table 2**.

The study also detailed the likely oxytetracycline breakdown process using fuel cells. According to (Wang *et al.* 2018), oxytetracycline and chlortetracycline were broken down into 3-hydroxy cyclohexanone as their degradation product begins with the extraction of both a hydroxyl and a hydrogen atom from the carbon atom [42, 43]. The dehydration of the chemical results in the creation of anhydrous oxytetracycline and chlortetracycline. After a series of processes, 3-hydroxycyclohexanone was formed, which was then transformed to CO2 and H2O by hydroxyl radical assault [62]. Sulfamethoxazole was identified to be another antibiotic from the wastewater [36], and was detected in seven wastewater plants in USA [30] and Hong-Kong [34] ranging between 0.05 g/L - 0.37 g/L and 5ng/L to 300 ng/L, respectively. *Paucibacter* sp. and *Filomicrobium* sp. were found to be capable of removing 89 percent of Sulfamethoxazole from wastewater [18]. At the end of the aerobic phase, six cycles of aerobic and anoxic cycles were repeated, resulting in the creation of a substantial quantity of nitrates, which were then eliminated *via* anaerobic procedures [18]. Likewise, (Lin *et al.* 2015) discovered that *Pseudomonas* sp. CE21 could degrade around 95% of the sulfamethoxazole antibiotic from doses of 0.1ppm of sulfamethoxazole [35]. Sulfamethoxazole was degraded into 3-amino-5methylisoxazole when Sulfamethoxazole was broken down in microbial fuel cells by combining electrical activity with microbial activity [44]. (Lin *et al.* 2015) proposed that further research be done to understand the organic compound breakdown mechanisms 35 better.

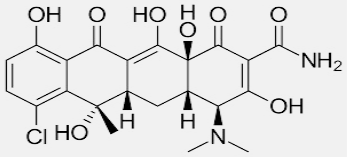
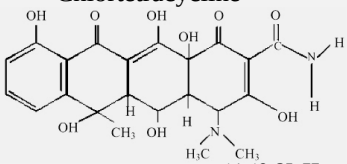
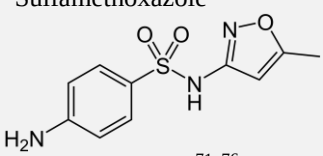
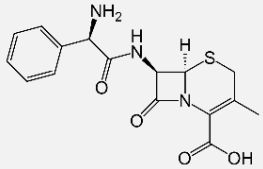
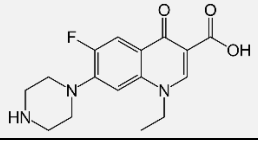
(Lin *et al.* 2015) recognized two Cefalexin-degrading strains of *Pseudomonas* sp., namely *Pseudomonas* sp. CE21 and *Pseudomonas* sp. CE22. *Pseudomonas* sp. CE22 can degrade over 92.1 percent of cefalexin after 24 hours of incubation in the presence of 1ppm cefalexin in the medium, while *Pseudomonas* sp. CE21 can eliminate 46.7 percent [35] **Table 2**. The cefalexin degradation capacity of *Pseudomonas* sp. CE 21 and *Pseudomonas* sp. CE22 did not change when the concentration of Cefalexin was increased to 10 ppm in both cases to determine the strains' maximal tolerating capacity, as determined by the study.

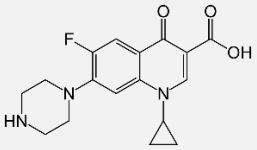
In contrast, (Lin *et al.* 2015) found that the presence of any other pharmaceutical at concentrations as low as 1ppm massively diminished the removal potency of Cefalexin by *Pseudomonas* sp. CE22, though not by *Pseudomonas* sp. CE21 [35]. *Pseudomonas* sp. CE 21 and *Pseudomonas* sp. CE22 both metabolized cefalexin by breaking it down into "2-hydroxy-3-phenyl pyrazine" as the degradation product [35]. Norfloxacin was detected in seven Hong Kong wastewater plants at concentrations varying between 35ng/L to 4000ng/L [34]. This confirms their presence in the wastewaters. According to (Parshikov 2012), norfloxacin was degraded by *E. coli*, *Pseudomonas* sp., *Microbacterium* sp., *Mycobacterium* sp., and *Streptomyces* sp. via site-specific hydroxylation [45] **Table 2**.

The study also indicated norfloxacin metabolism, which includes both N-acetylation and splitting the antibiotic compound's piperazine ring. *Mycobacterium gilvum* degraded norfloxacin in the effluent to generate N-acetyl norfloxacin, 6-hydroxynorfloaxcin, 8-hydroxynorfloaxcin, and desethylene N-acetyl norfloxacin as by-products, whereas *Microbacterium* sp. degraded norfloxacin to generate N-acetyl norfloxacin (same by product of metabolism of norfloxacin by *Microbacterium* sp. and *Mycobacterium gilvum*) [45]. *Trichoderma viride* was cultured in a medium containing norfloxacin, which formed conjugates when the antibiotic reacted with the cyclopentanone secondary metabolite of *Trichoderma viride* [45, 63]. Likewise, degradation of Norfloxacin by *Pestalotiopsisguepini* generated by-products such as N-acetyl norfloxacin, N-formyl norfloxacin, desethylene N-acetyl norfloxacin, and 7 – amino – 1 – ethyl – 6 – fluoro - 4oxo - 1, 4-dihydroquinoline-3-carboxylic acid [45, 63].

Norfloxacin has complete structural similarity with ciprofloxacin, except ciprofloxacin contains an additional N-cyclopropyl group. The presence of ciprofloxacin in wastewater were confirmed when they were detected and isolated from seven different wastewater plant of Wisconsin of USA at concentrations varying between 0.04 µg/Lto 0.14 µg/L [30]. Ciprofloxacin degrading capacity was discovered in *Umbelopsis rammaniana*, that metabolized ciprofloxacin to yield N-acetyl ciprofloxacin [46]. Furthermore, *Pestalotiopsis guepini* can break down ciprofloxacin into N-formyl ciprofloxacin, N-acetyl ciprofloxacin, 7-amino – 1 – cyclopropy l - 6 – fluoro - 4-oxo-1,4-dihydroquinoline-3-carboxylic acid, as well as desethylene N-acetyl ciprofloxacin [47]. Tinea versicolor was also identified as having the ability to degrade ciprofloxacin by converting it to the molecules 8-hydroxy ciprofloxacin, 7-amino-1-cyclopropyl-6-fluoro-4-oxo-1, 4-dihydroquinoline-3-carboxylic acid and desethylene ciprofloxacin [50].

TABLE 2: REMOVAL EFFICIENCY OF MICROORGANISMS FOR ANTIBIOTICS FROM ANTIBIOTIC-PRODUCING PHARMACEUTICAL INDUSTRY WASTEWATER

Name of Antibiotics	Name of Degrading Microorganisms	Antibiotic Source	Removal Efficiency (%)	Time
Oxytetracycline [51-57] 	Closed circuit Microbial fuel cell; *Stenotrophomonas sp. Azospirillum sp. Pandoraea sp.* Open circuit Microbial fuel cell: *Stenotrophomonas sp. Burkholderia sp. Pandoraea sp.*	Microbial fuel cells	78%	7 days
Chlortetracycline [58-63] 	Closed circuit Microbial fuel cell: *Petrimonas sp. Azospirillum sp. Dokdonella sp*. Open circuit Microbial fuel cell: *Petrimonas sp. Burkholderia sp. Stenotrophomonas sp*	Microbial fuel cells	74.2%	7 days
Sulfamethoxazole [14, 18, 35, 77] 	Paucibacter Filomicrobium *Paucibacter sp. Filomicrobium sp.Pseudomonas* sp. CE21	Bioreactor, Bioreactor Sludge (Activated)	89% 89% 95%	5 days 5 days 24 hours
Cefalexin [71, 76] 	*Pseudomonas* sp. CE21, *Pseudomonas* sp. CE22	Sludge (Activated) Sludge (Activated)	46.7% 92.1%	24 hours 24 hours
Norfloxacin [77, 80] 	*Escherichia sp.Pseudomonas sp. Microbacterium sp. Mycobacterium gilvum, Streptomyces sp. Trichoderma viride, Pestalotiopsisguepini*	Wastewater treatment plant	ND	-

Ciprofloxacin [81, 82] 	*Umbelopsis rammaniana, Pestalotiopsisguepini, Tinea versicolor*	Wastewater treatment plant	ND	-

*ND: Not Determined

DISCUSSION: As can be observed from the above, additional study is required to optimise the removal efficiency of antibiotics and heavy metal ions found as pollutants in the effluents of pharmaceutical companies that manufacture antibiotic drugs. The removal efficiency (%) of Cadmium (Cd) and Copper (Cu) by *Chaetoceros calcitrans* could not be determined [49]. However, no such published results are available that have determined the removal efficiency (%) of Cd and Cu by *Chaetoceros calcitrans.* However, the study conducted by (Pratiwi *et al.* 2019), calculated the Bioconcentration Factors (BCF) based on the capacity of absorbance of heavy metal; copper and cadmium. The researchers identified the relationship between BCF and the concentration of heavy metals to be inversely proportional to each other, indicating their ability to accumulate heavy metal ions even at low concentrations [49]. But in the case of pharmaceutical firms producing copper and cadmium at concentrations above normal levels, *i.e.,* 1.9 ppm approx., the biosorption capacity of such metals by *Chaetoceros calcitrans* will significantly decrease [49]. Concerning the event that antibiotics are found in pharmaceutical company wastewater effluents, more studies need to be conducted to identify the potential removal efficiency (%) of *Escherichia* sp., *Pseudomonas* sp., *Microbacterium* sp., *Mycobacterium gilvum, Streptomyces* sp., *Trichoderma viride, Pestalotiopsis guepini* fornorfloxacin and *Umbelopsis rammaniana, Pestalotiopsisguepini, Tinea versicolor* for ciprofloxacin. Superbug strains could be created *in-vivo* by isolating genes from different microorganisms such that one microbe could breakdown several antibiotic drugs or heavy metal ions. This would be extremely advantageous for the pharmaceutical industries, enabling them to save cost and time.

Discussion on the Potential of *Bacillus* sp. to Remove Heavy Metals from Effluents of Antibiotic Producing Pharmaceutical Industry: *Bacillus* sp. is particularly efficient for biodegradation purposes, as evidenced by the preceding studies, as it can biodegrade numerous heavy metals. *Bacillus firmus* could biodegrade Copper (74% biodegradation efficiency), Zinc (69.8% biodegradation efficiency), *Bacillus cereus* can biosorb copper (50.32mg/g biodegradation efficiency), strain NSPA8 of *Bacillus cereus* can biosorblead (98.3% removal efficiency). According to scientific literature, *Bacillus subtilis* is likewise capable of biosorption of Fe; however its removal efficiency could not be confirmed. However, more research is needed to identify the precise removal efficiency of iron by *Bacillus subtilis*.

Discussion on the Potential of *Pseudomonas* sp. to Remove Antibiotics from Pharmaceutical Industry Wastewater: *Pseudomonas* sp. is an unique genus of bacteria capable of breaking down a wide range of antibiotic drugs.*Pseudomonas* sp. CE 21 can digest Sulfamethoxazole (Biosorption efficiency: 95%) and Cefalexin (Biosorption efficiency: 95%). (Biosorption efficiency 46.7%). Additionally, the strain *Pseudomonas* sp. CE 22, can biodegrade Cefalexin (Biosorption efficiency 92.1 %) [35].

Both strains of *Pseudomonas* sp., *Pseudomonas* sp. CE21 and *Pseudomonas* sp. CE22, decomposed cefalexin by producing "2-hydroxy-3-phenyl pyrazine" [35]. In order to investigate the effect of other drugs on the degradation capability of *Pseudomonas* sp. CE21 and *Pseudomonas* sp. CE22, the study included a combination of nine other medications that are commonly found in wastewater at concentrations of 1ppm each. *Pseudomonas* sp. CE21 exhibited no significant changes in Cefalexin degradation capacity after a day, whereas *Pseudomonas* sp. CE22 showed a substantial drop in biodegradation efficiency in the presence of other pharmaceutical waste fluids [35]. It can be assumed that the wastewater from such pharmaceutical firms will always contain a mixture of all medications, not just cefalexin. As a result, the strain CE21 can be deemed more efficient in

biodegradation than CE22, because the presence of other pharmaceutical medications in the effluents has no effect on removal efficiency.

Discussions on the Reusage of Wastewater from Antibiotic Producing Pharmaceutical Industry: In accordance with the guidelines by the World Health Organization (WHO) for reusing wastewater, first, the treated wastewater should have no presence of faecal coli forms, secondly there should be the absence of cases of enteric diseases in the exposed population, and thirdly annual risk assessment should be done with the help of a quantitative microbial risk assessment model. Wastewater is cleansed and reused in drought-prone locations and countries, such as the Middle East, where fresh water is scarce. In such circumstances, wastewater should be free of any antibiotics or heavy metal ions, as these substances may cause bacteria to develop resistance to particular antibiotics, or heavy metal ions may harm human populations, crops and animals. Antibiotics in wastewater should be detected in very low quantities by wastewater treatment plants, as some antibiotics may be diluted, making detection difficult [37].

The effluent is processed and then used in agriculture. Considering these conditions, wastewater should always be free of pollutants that could cause crops to absorb antibiotics. According to a study (Wu *et al.* 2012), spinach, lettuce, and tomatoes are vegetables that absorb Sulfamethoxazole when treated wastewater is used. Sulfamethoxazole is taken up by spinach and lettuce at concentrations below the technique limit of detection, whereas tomatoes uptakes them at concentrations of 9.7 ± 0.6 ng/g of dry weight, making it a matter of concern since such veggies are frequently consumed uncooked and hence may eventually reach humans [64]. Antibiotic resistance microorganisms have emerged due to inappropriate and excessive antibiotic use in humans and animals, which may have negative environmental consequences. Antibiotic dosage below the prescribed level, *i.e.,* subtherapeutic levels, for an extended period causes bacteria to become resistant [8]. In Oman, a study (Al-Bahry 2012) discovered the prevalence of antibiotic-resistant bacterial strains in wastewater for Sulfamethoxazole with a resistance capability of up to 95% [7].

Antibiotic-resistant bacteria may come into touch with crops, posing a threat to agriculture [8]. As a result, pharmaceutical companies should exercise extreme caution when dumping wastewater into nearby bodies of water. In addition, wastewater treatment plants should collaborate to identify antibiotics and heavy metal ions in wastewater, even in extremely low quantities.

Future Applications for Product Recovery from Different Pharmaceutical Industry Wastewater:

Bio-stimulation or Bioaugmentation: In the process of bio-stimulation, the growth conditions of the microorganism can be altered by altering the pH, nutrients, oxygenation or by adding biosurfactants. This may allow the microbes to withstand stress from the surrounding medium and adapt to it.

Widening the use of Genetically Modified Microorganism: Genetically modified organisms can have better biodegradation capacities along with better tolerance to heavy metals, antibiotics etc. Such can also degrade multiple antibiotics, drugs, or heavy metals in one go. Such can be brought in by introducing stress-resistant genes into the genome of the microbes, leading to the development of new strains.

CONCLUSION: This review represents the use of microorganisms to treat effluents from antibiotic-producing pharmaceutical industries. The treatment includes the treatment of several heavy metal ions as well as antibiotics which are commonly found in wastewater from such pharmaceutical industries.

The harmful phenomena exhibited by the pollutants is resulting in severe global environmental issues, which shall be increasing in the near future if not addressed properly. Several studies have been performed to know the constituents of the effluents and microorganisms involved in their biosorption. Such industries will benefit from this regarding efficient management of effluents before discharging them into water bodies. Also, the biomass generated from treating the effluents can be used later. This technique can prove itself economical for every pharmaceutical industry, whether small or large because an industry can only carry out a process if it seems economical. Such pharmaceutical industries should also focus on

producing superbugs which will make this effluent treatment process more economical to them. Also, the microorganisms can be used again and again several times.

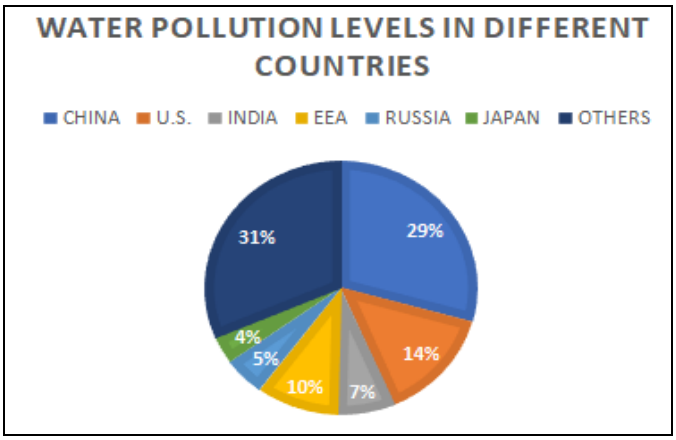


FIG. 1: COMPARISON OF WATER POLLUTION AMONG SEVEN DIFFERENT COUNTRIES

From **Fig. 1**, it is evident that India is still behind several developed nations regarding water pollution. Since the situation still in control, stricter regulations should be implemented to decrease the level of pollutants in the wastewater. The drainage of harmful effluents from the antibiotic-producing pharmaceutical industries into nearby water bodies threatens the aquatic systems and the humans using them. Heavy metal ions are known to be a major cause of diseases of skin in human beings and animals. Further, antibiotics present in wastewater from pharmaceutical industries are discharged into the water bodies and ingested by fishes, humans and animals, which identifies it as a major matter of concern. Recent advancements in this technique should be implemented and popularized, emphasizing the production of genetically modified microbes to produce superbugs that could degrade several pollutants from the effluents of the pharmaceutical industry producing antibiotic drugs at once. This shall result beneficial for the pharmaceutical industries.

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