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REMEDIATION OF PHARMACEUTICAL RESIDUES IN DRINKING WATER BY LOCALLY ISOLATED FUNGUS: AN ECOFRIENDLY APPROACH

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Abstract

Water pollution is a substantial threat to humans. Micropollutants like pharmaceuticals have been found in almost every source of drinking water. They are so persistent that even waste water treatment plants are incapable to remove them properly from waste water and ultimately their residues approaches the surface water through effluents. A current investigation focuses on bioremediation of selected pharmaceutical residues in drinking water using locally isolated fungal species. Five commonly found drugs such as ciprofloxacin, aspirin, ibuprofen, fenofibric acid and carbamazepine in drinking water (tap, tube well and hand pump) samples were analyzed and treated with *Aspergillus niger* as it was found as most resistant and active species for removal of pharmaceuticals. Degaradation rate of drugs were checked for 12 days under optimized conditions. The samples were taken after every 2 day and analyzed on HPLC. Disappearance of ipubrufen and carbamazepine was noted for maximum time i.e., 12 days while for aspirin degradation was observed till 8 days. pH of liquid media was found to be unstable during degradation of compounds and detected as acidic for all except carbamazepine. Further investigations are suggested for the determination of capabilities of fungal species regarding bioremediation of organic micropollutants.

Keywords: Bioremediation, *Aspergillus niger*, ipubrufen, carbamazapene, organic micropollutants, drugs

1. INTRODUCTION

Contamination of groundwater is generally caused by human activities in which contaminants prone to percolation are collected and deposited on or below the surface of the soil (Muralikrishna and Manickam, 2017). Micropollutants, when continuously launched with wastewater effluents, can lead to long-term risks due to the fact the contaminants persists and can even structure new combos in water. Micropollutants are bioactive contaminants that can't be totally eradicated with standard wastewater remedy strategies and that are no longer completely biodegradable (Benner *et al*., 2013).

Pharmaceuticals have been found in almost every source of drinking water (Carmona *et al*., 2014). Determining and researching the destiny of pharmaceutical products in water has been a subject of growing research interest since past many years. Such compounds are emitted primarily by municipal sewage and many of them, due to their soluble nature

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and low degradation at sewage and drinking water treatment plants, can disperse further through the water cycle (Rodil *et al*., 2012). Although, majority of pharmaceuticals stay for a very less time in atmosphere due to processes like biodegradation, hydrolysis, UV etc., but still their residues are found everywhere (Ribera *et al*., 2014). The levels of medicines in water present a big challenge to human health due to their permanence in waste water systems and inefficiency waste water treatment plants to remove those (Gauthier *et al*., 2010).

Microbes are active in natural purification mechanisms in environments as they can remove toxins by co metabolic and /or metabolic routes. Biodegradation is known to be the most crucial phenomenon to remove certain xenobiotics like pharmaceutical products (Topp *et al*., 2013). Fungi are known as microorganisms, performing significant roles as decomposers, pathogens or mutualists in nature. Application of fungi, generally, *Penicillium species* and *Aspergillus niger* has been explored as an innovative method to treat contaminants like pharmaceutical and personal care products (Rodarte *et al*., 2011).

Inadequate and unsafe water quality for drinking purposes in Pakistan imposes a huge threat to health of population. Release of hazardous substances into the water sources from urban areas and manufacturing facilities without any processing impairs the quality of water and causes detrimental effects on human health (Daud *et al*., 2017). Poor water quality in Pakistan has been attributed to the unchecked and wrong dumping of industrial and municipal waste and careless use of chemicals in agriculture and other attributes of subsistence (Azizullah *et al*., 2011).

Keeping in view, the perspective of present study is designed to deal with the degradation of common occurring pharmaceutical residues in drinking water using fungi. Considering that wastewater treatment plants are not specially designed to remove them, fungi and their enzymes are among the most promising solutions to the problem. Fungus species efficient in degrading these micro pollutants will be isolated and selected using culture enrichment technique. The proposed study also attempts levels of degradation achieved through fungal bioremediation analysis.

2. MATERIALS AND METHODS

Present study focused on bioremediation of pharmaceutical residues in drinking water samples collected from drinking water sources i.e., tap water, hand pump and tube well of the residential areas around pharmaceutical industrial estate. The samples were collected using coherent protocols and sampling was conducted on consistent days of the week, samples were collected biweekly for a period of 4 months. About 150 samples were collected from 21 selected sites. The composite samples were subsequently collected in pre cleaned and dried amber glass-bottles. Analysis for pharmaceutical residues was done within 36 hours of collection using High Performance Liquid Chromatography (HPLC). Analysed drugs were Aspirin, Ibuprofen, Fenofibric acid, Ciprofloxacin and Carbamazepine (Table. 1).

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Table 1: List of identified drugs in the water samples of selected area

Pharmaceutical classes	Pharmaceutical drugs	Molecular Formula	Molecular wt. (g/mol)
Antibiotics	Ciprofloxacin	C17H18FN3O3	385.8
Anti-inflammatory	Aspirin	HC9H7O4	180.16
Non-opioid analgesics	Ibuprofen	C13H18O2	206.28082
Lipid regulators	Fenofibric acid	C17H15ClO4	318.75
Antiepileptics	Carbamazepine	C15H12N2O	236.27

2.1. Fungal isolation from surface water of the canal

Potato dextrose Agar (PDA; Oxoid, Pk) having 5mg/L of the drugs mixture was used to isolate the fungal strain from the surface water of the industrial site. 100µL of wastewater was spreaded on the PDA plates having the pharmaceutical drugs. PDA plates were made by using pour plate method (Sheetal *et al*., 2020). The plates were incubated for 7 days at 25^{o}C. After this time, the isolates appeared on all the plates were re-streaked on new agar plates having drug residues. These were further allowed to grow for 7 days at 25^{o}C.

The colony size (%) of the isolated fungi was determined. The fungal growth was then estimated quantitatively by taking images of mycelia by light microscope annexed with Nikon camera. The diameter on the agar plate was said to be 100% (90mm) and colony size was determined as per. The formula employed was as follows;

$$colony\ size\ (\%) = \frac{colony\ size\ in\ mm \times 100}{plate\ agar\ size\ (90mm)}$$

2.2. Removal Assay for pharmaceutical residues

The removal efficiency was determined for the pharmaceutical drugs under sterile conditions and the pH of the medium adjusted to pH 5.5-6.5 (IM HCl acid used). Here, surface water sample was used as negative control.

Initially, 250mL glass flasks received 50mL of the sterile synthetic wastewater media composed of 0.2g K_2HPO_4, 0.5g $MgSO_4$, 0.8g KH_2PO_4, 0.2g yeast extract in 1L of Milli-Q water, 5mg/L of selected pharmaceutical residues and fungal inoculum from the newly re-streaked plates. The flasks were incubated in the shaking incubator (150rpm) for 10 days at 25^{o}C. The concentrations were then determined periodically after incubation periods of 0, 3, 5, 8 and 10 days (Kähkönen *et al*., 2017). Analysis of the residues was conducted on High Performance Liquid Chromatography (HPLC) following the guidelines of Fatoki et al. (2018).

2.3. Biosorption Test

Fungal biomass of the isolates was allowed to grow in the PD medium (without agar) and incubated in the shaking incubator (50rpm) for 5 days at 25^{o}C. Half of the flasks that received the fungal inoculum were double autoclaved to kill the fungal cells (dead fungal cells). Two additional negative controls were prepared i.e., one without the pharmaceutical drugs and other without fungi were also analyzed in parallel. The pharmaceutical compounds were added in the bottles without fungi and one with dead

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and alive fungi. All the samples were incubated on shaking incubator (50rpm) at 25°C. Samples were then analyzed for degradation at 0, 3, 5, 8, 10, 12, 16 days.

The above experiment was quality controlled to observe the link of bioremoval as induced by fungi. Analysis of the residues was conducted on HPLC.

3. RESULTS

3.1. Identificaion of fungal species

To identify the fungal species, the water was streaked on the PDA plates. As shown in the figure 1 and 2 that initial screening revealed a lot of *Apergillus sp*. started to flourish. Along with the *Aspergillus sp*., *Mucor sp*. was also observed on the plate.

The 10 different plates prepared from the 10 sites showed the abundance of *Aspergillus sp*. as apparent from the colony colour, type and shape. Since, *Aspergillus niger* was suspected to be the most abundant species (when colony size and other characteristics were studied and compared) so the pure sample of *Aspergillus niger* was purchased from the Fungal Bank and further grown in the PD liquid media for the pharmaceutical residues degradation assay (Fig.3). Experiment was allowed for the 12 days under optimized conditions. The samples were taken after every 2 day and analyzed on HPLC.

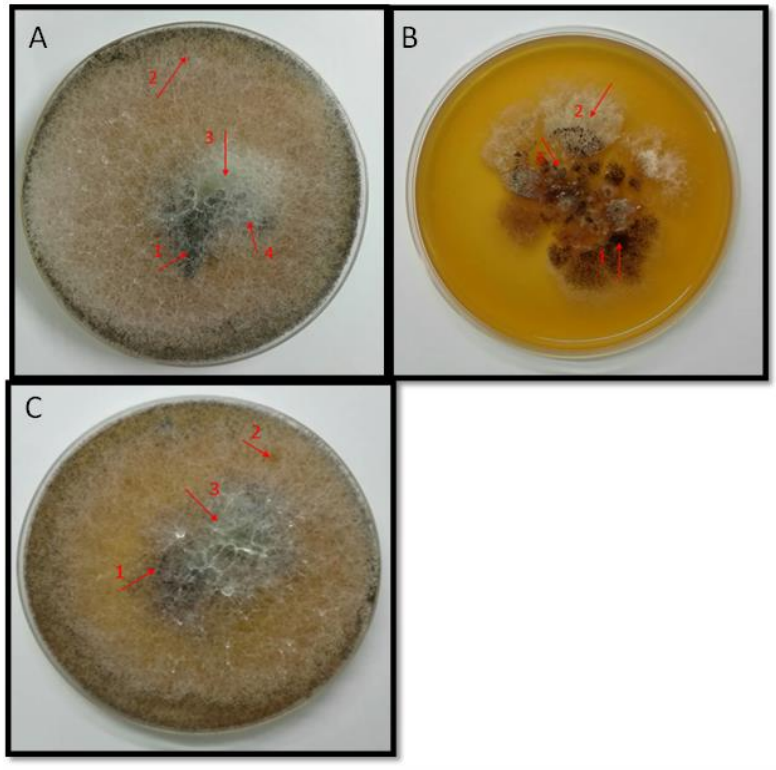

Figure 1: Three different plates as obtained from spreading the contaminate water from the selected sites. Microscopic evaluation revealed mostly to be *Aspergillus niger*, *Apergillus fumingitus* and *Mucor sp*.

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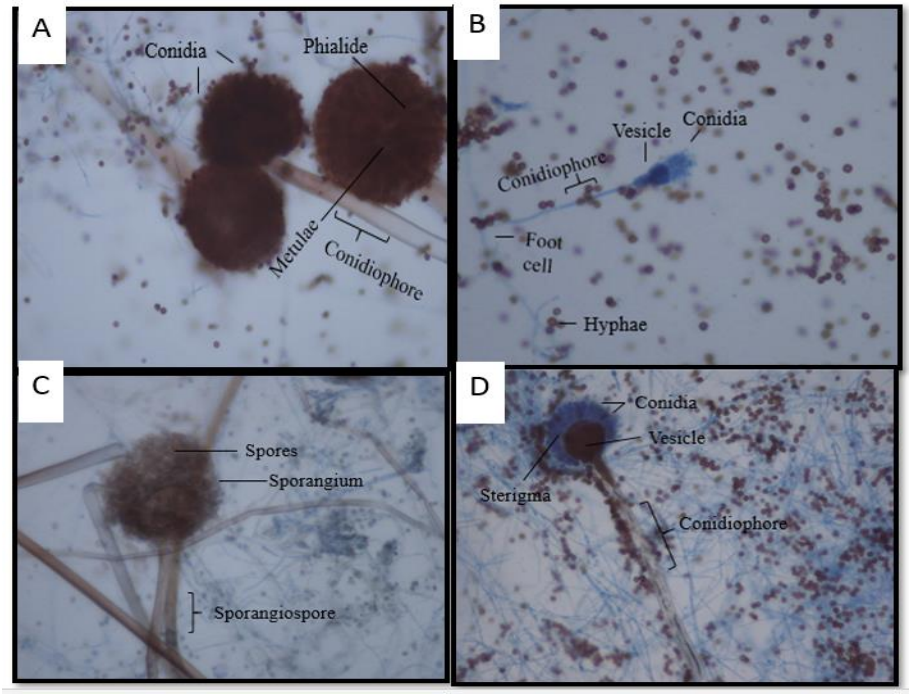

Figure 2: (A) *Aspergillus niger* B) *Mucor sp*. C) *Aspergillus fumingitus* D) *Aspergillus flavus*

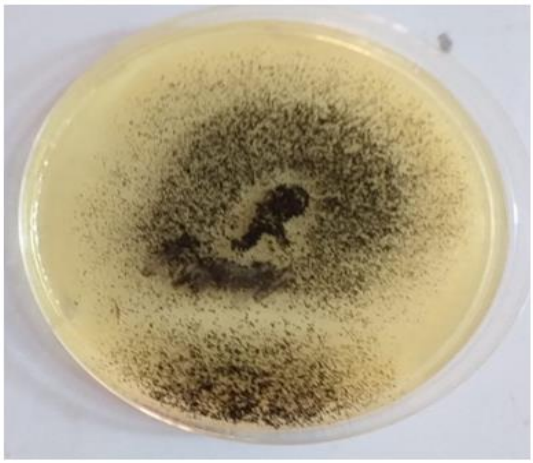

Figure 3: Pure culture of *Aspergillus niger* obtained for the experiment.

4.3.2. Degradation rate of different pharmaceutical residues using *Aspergillus niger*

Degradation rate of Ciprofloxacin showed that as the time preceded the compound started to disappear. The change in pH of the medium was also noted. The pH turned to be more acidic and maximum degradation was obtained for 10 days. After 10 days the degradation turned static (Fig. 4). Figure 5 depicts the degradation rate of aspirin. Initially, rapid degradation was observed for 8 days but later it turned static. The pH of the medium declined and tends to be more acidic.

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Examination of degradation rate of ibuprofen suggested that as the time exceeded the degradation increased until 12 days. The pH was also observed to be unstable and dropped in the medium (Fig. 6). Continuous decrease in concentration of Fenofibric acid was observed until 10 days. The pH of the medium was remained unstable and gradually dropped down (Fig. 7).

Degradation of carbamazepine suggested that as the time exceeded the degradation exceeded until 12 days. The pH was observed as unstable and raised in the medium (Fig. 8).

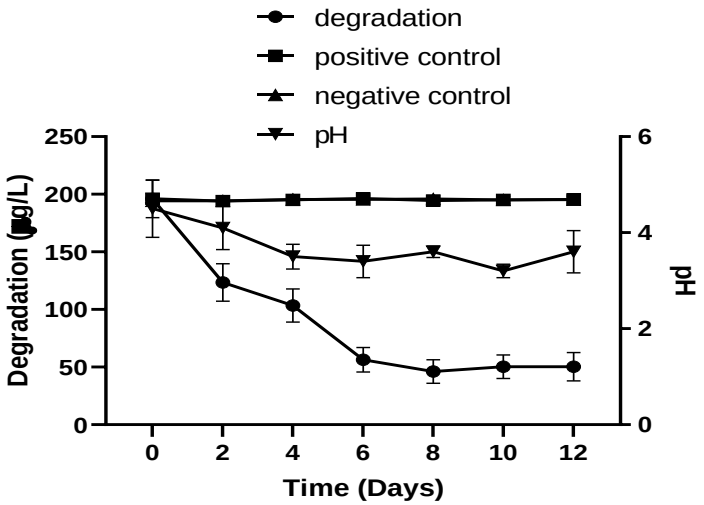

Figure 4: Rate of Ciprofloxacin degradation from the liquid media over a period of 12 days under optimized conditions of temperature and light.

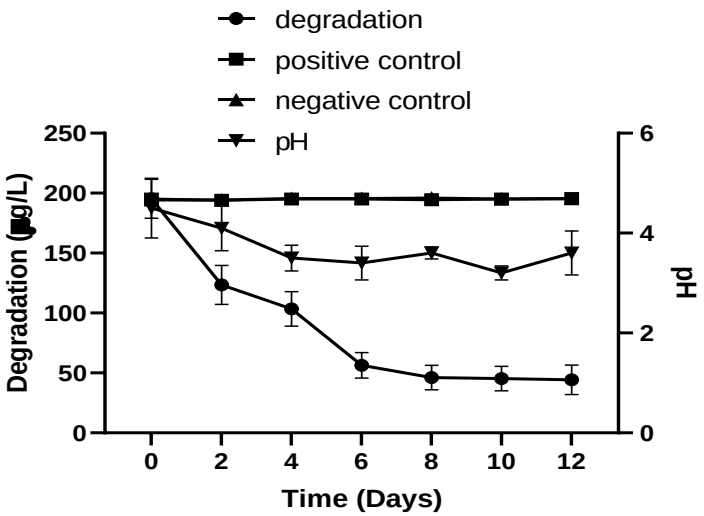

Figure 5: Rate of Aspirin degradation from the liquid media over a period of 12 days under optimized conditions of temperature and light.

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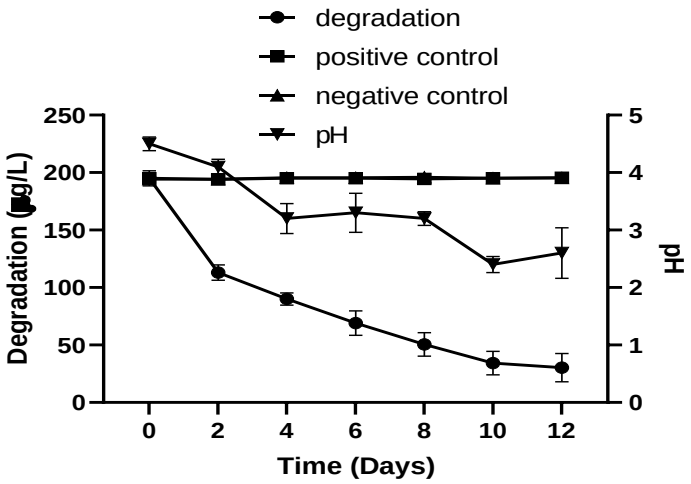

Figure 6: Rate of ibuprofen degradation from the liquid media over a period of 12 days under optimized conditions of temperature and light.

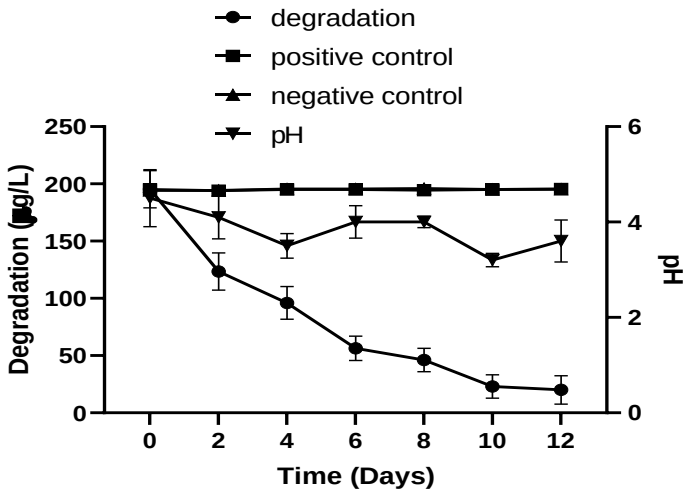

Figure 7: Rate of Fenofibric acid degradation from the liquid media over a period of 12 days under optimized conditions of temperature and light

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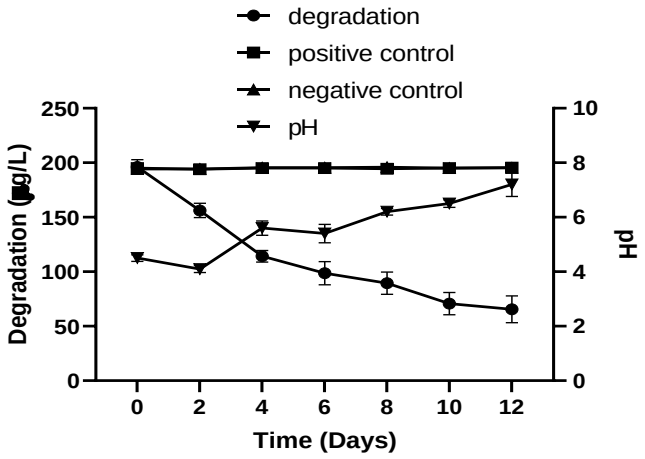

Figure 8: Rate of Carbamazepin degradation from the liquid media over a period of 12 days under optimized conditions of temperature and light

4. DISCUSSION

Pharmaceutical are emerging organic pollutants which have been continuously adding into our water systems due to their inescapable usage by humans and veterinaries. Increasing demand of pharmaceutical resulted in rapid increase of drug making units which have become the major contributors of polluted waters into water bodies. Parent molecules as well as their derivatives are part of waste water streams in form of human excreta. Untreated or partially treated waste water ultimately enters into ground and surface water streams presenting great threat to water aquatic life and drinking water quality. To avoid all this there is a dire need of developing comprehensive and organized systems which ensure the proper treatment of industrial effluents and sewage waste water. Moreover, conventional treatments methods need to switch with innovative, efficient and cost-effective options. Biodegradation is a viable choice to treat pharmaceutical compounds effectively.

The detection of pharmaceutical active chemicals (PhAC) such as aspirin, ibuprofen, fenofibric acid, ciprofloxacin and carbamazepine in the drinking water supplies necessitates a thorough understanding of the different physiochemical characteristics, as well as the best conditions for pharmaceutical separation and estimation. The employment of a UV detector in high-performance liquid chromatography (HPLC) has considerably aided the detection of compounds in pharmaceuticals in particular (Beatriz *et al*., 2020).

Current investigation found the presence of five selected drugs in water samples from residential areas around Pharmaceutical industries. This presence is mainly attributed to the contamination of surface and ground water aquifers with waste water effluents from medicine industries. Even if discovered in tiny amounts, the persistence and pharmokinetics of these contaminants make them dangerous to human health. One of the study conducted by Ashfaq et al. (2017) evaluated the same aspects. They detected

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eleven commonly formed medicines in several environmental metrics near pharmaceutical formulation plants in Shiekhupura, Lahore, Pakistan.

Since conventional wastewater treatment facilities are not fully equipped for the treatment of pharmaceuticals so degradation of these pollutants has become a matter of grave concern (Żur *et al*., 2018). Microorganisms are important players in the biological breakdown of dangerous substances in the environment. Mycoremediation is an emerging treatment method for organic contaminants. Unspecific peroxygenases, lipase, manganese peroxidase, laccase and esterase are important enzymes which aids the degradation of micropollutants such as pharmaceuticals and personal care (Karich *et al*., 2017).

Present study aimed to treat selected pharmaceutical residues using fungal species isolated from water. *Aspergillus niger* was found to be most resistant and effective in treating selected residues. These findings are supported be the findings of a study done by Naghdi and coworkers in 2018 in which they explored the tremendous abilities of various species of *Aspergillus* for degrading pharmaceuticals in waste water. It is also evident from literature that colony making process and intricate physiology of mycelial fungi i.e., *Aspergillus niger* make them significantly effective in removing pharmaceuticals and allow them to survive even in harsh environment (Dalecka *et al*., 2021; Schuster *et al*., 2002; Rana *et al*., 2017).

Disappearance of drugs using *Aspergillus niger* inoculum was monitored for 12 days under optimized conditions. Concentrations were measured after every 2 day. Results showed degradation of ipubrufen and carbamazepine till twelfth day, which was maximum noted time while for aspirin disappearance was observed till 8 days. The results are supported by the findings of one of the similar study which assessed the simultaneous elimination of various pharmaceuticals including diclofenac, ibuprofen and carbamazepine using different species of already isolated fungi i.e., *Aspergillus niger, Rhizopus microsporus*, *Trichoderma Mucor circinelloides* etc. Maximum disappearance (87%) of carbamazepine was attained by *R. microsporus* at 10 days. Diclofenac was removed almost full by all fungi species including *Aspergillus niger* after a day whereas ipubrufen was almost 100% removed after 2 days of experiment. It was also emphasized that besides basidiomycetes, zygomycetes and ascomycetes also have significant capacities to degrade organic pollutants (Kasonga, *et al*., 2021).

Experiments for the investigation of degradation rate of selected pharmaceuticals were conducted under controlled conditions of pH, temperature and light and found to be very crucial in expediting removal of pharmaceuticals. pH of liquid media was found to be unstable during degradation of selected drugs and detected acidic for all except medium of carbamazepine. These observations are depictive of the fact that environmental factors such as the, moisture, pH and temperature played an important role in the distribution of mycoflora. These were the main factors affecting the fungal population and diversity (Gaddeyya *et al*., 2013).

Numerous studies have been depictive of the extraordinary strength of many species of fungus that have been attested for effectively treating pharmaceutical residues. However,

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their long growth cycle and spore formation make their usage limited in treatments (Zhuo and Fan, 2021). Continuous lowering of the levels of aspirin, ibuprofen, fenofibric acid, ciprofloxacin and carbamazepine has been observed during experiments of present study. Degradation of fenofibric acid was noted till 10 days. These findings inferred the active participation of *Aspergillus niger* in biotransformation of these compounds. This specie has been known since long for the ability of oxidative enzymes to transform a wide range of obstinate compounds. Moreover, distinct characteristics of fungus physiology and unique colony forming aspects make them strong to halt abrupt changes in environmental conditions and yet breakdown of complex carbon compounds competently (Anastasi *et al*., 2013).

5. CONCLUSION

Pharmaceutical have received a lot of attention in recent years because of their constant discharge into natural waters. Conventional techniques are attested as inadequate for removing organic micropollutants. Mycoremediation have been shown to be a cost-effective, ecofriendly and innovative option means of removing a wide range of toxins from contaminated environments with pharmaceuticals. In the determination of removal efficiency of selected pharmaceutical products, *Aspergillus niger* has been observed to be very effective in removal of aspirin, ibuprofen, fenofibric acid, ciprofloxacin and carbamazepine, however, the biomass of the organism need continuous sustenance provided through continuous supply of optimized conditions. There is an urgent need to observe the active enzymes which are involved in the degradation and consumption of these compounds from the inoculum. The stability of these enzymes can then be determined and used in a system where maximum degradation of the PhACs can be achieved.

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