

RESEARCH ARTICLE

APPLICATION OF ANAEROBIC BIOTECHNOLOGY FOR PHARMACEUTICAL WASTEWATER TREATMENT

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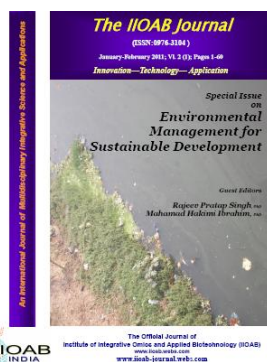
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ABSTRACT



The wastewater generated from pharmaceutical industry generally contain high organic load and the treatment is primarily carried out using two major types of biological methods; aerobic and anaerobic. However, due to high strength, it is infeasible to treat some pharmaceutical wastewater using aerobic biological processes. As an alternative, an anaerobic process is preferred to remove high strength organic matter. Anaerobic wastewater treatment is considered as the most cost effective solution for organically polluted industrial waste streams. In particular the development of high rate systems, in which hydraulic retention times (HRT) are uncoupled from solids retention times (SRT), has led to a worldwide acceptance of anaerobic wastewater treatment. In this paper, literature on anaerobic digestion, anaerobic reactor technology and existing anaerobic treatment of pharmaceutical wastewater are presented. In addition, fate of pharmaceuticals in the environment was also discussed in brief. A case study of a laboratory investigation into the treatment of pharmaceutical wastewater containing the antibiotic Tylosin in an anaerobic reactor was also given. Specifically, it was determined whether the anaerobic reactor could be used as a pre-treatment system at an existing pharmaceutical production plant. The performance of the reactor treating real pharmaceutical wastewater at various organic loading rate (OLR) was investigated and showed efficient substrate removal at low OLRs ($0.43 - 1.86 \text{ kg COD.m}^{-3}.\text{d}^{-1}$) by promoting efficient chemical oxygen demand (COD) reduction (70 – 75%). Under these conditions, an average of 95% Tylosin reduction was achieved in the UASR. However, increasing the OLRs to $3.73 \text{ kg COD.m}^{-3}.\text{d}^{-1}$ by reducing the hydraulic retention time (HRT) (4 – 2 d) reduced the COD removal efficiency (45%). Changes in the organic loading affected the treatment performance of the anaerobic reactor, and at high OLRs, it was not able to withstand the short HRT, probably due to the complexity of pharmaceutical wastewater.

Keywords: Anaerobic digestion; antibiotic; pharmaceutical wastewater; tylosin; UASR

[1] INTRODUCTION

1.1. Anaerobic digestion

In the past, aerobic processes were very popular for biological treatment of wastewater in the 1960s. However, the energy predicament in the early 1970s brought about a significant change in the methodology of wastewater treatment. Energy preservation in industrial processes became a major concern and anaerobic processes rapidly emerged as an acceptable alternative.

One of the important advantages of anaerobic digestion is the energy production during the process in the form of methane. Moreover, when high loading rates are accommodated, the area needed for the reactor is small. The sludge production is low, when compared to aerobic methods, due to the slow growth rates of anaerobic bacteria [1].

Figure–1 illustrates the advantage of anaerobic system in relation to aerobic treatment [2]. In aerobic process around 40 – 50% of biological stabilization take place, with its consequent

conversion into CO₂. The sludge production and non degraded material in aerobic system is around 50 – 60% and 5 – 10%, respectively. However, in anaerobic system most of the biodegradable material is converted into biogas (around 70 – 90%), and only small portion of the organic material converted into sludge (about 5 – 15%). The material not converted into biogas leaves the reactor as non degraded material (around 10 – 30%). It is notable that the production of methane gas and the very low production of solids is the main advantage of anaerobic treatment.

Anaerobic wastewater treatment is considered as the most cost-effective solution for organically polluted industrial waste streams [3]. Toxic and recalcitrant wastewaters, that were previously believed not to be suitable for anaerobic processes, are now effectively treated. Accordingly, effluents from manufacturing operations in the pharmaceutical industry, such as antibiotic formulation, usually contain recalcitrant compounds. The following section discusses briefly the effluent from pharmaceutical industry.

1.2. Effluent from pharmaceutical industry

The pharmaceutical manufacturing industry produces a wide range of products to be used as human and animal medications. Manufacturing can be characterized by five main processes; fermentation, extraction, chemical synthesis, formulation and packaging [4]. Each of these steps may generate air emissions, liquid effluents and solid wastes. Liquid effluents resulting from equipment cleaning after batch operation contain toxic organic residues. Their composition varies, depending on the product manufactured, the materials used in the process, and other process details. Typically, pharmaceutical wastewater is characterized by high COD concentration, and some pharmaceutical wastewaters can have COD as high as 80,000 mg.L⁻¹[5]. Pharmaceuticals pose potential risks to the aquatic environment such as endocrine disrupting and side effects since they initially cause specific biological effects [6, 7]. Furthermore, wastewaters produced from antibiotic manufacture and formulation, generally contain high levels of soluble organics, many of which are recalcitrant [8]. If these compounds are not removed by one-site treatment they will be discharged to sewage treatment plants (STPs). This then eventually could disturb the biological process and the microbial ecology in the STP and the receiving surface waters [6, 7, 9–13].

Widespread work into the occurrence and fate of pharmaceuticals in the environment has been carried out in recent years [14–20]. The aim of the majority of this work has been to identify particularly persistent substances. In addition, the quantities in which they occur in surface waters and wastewater effluents and the eventual long-term effects they may have in the aquatic environment. Essentially, the detection of pharmaceuticals such as antibiotics in the environment has raised concern about potential human health effects. Pharmaceuticals can enter the aquatic environment through the sewage treatment systems when they are excreted by people, or if they are disposed in the home [21]. They can also enter sewage treatment works or

watercourses as a result of discharges from pharmaceutical manufacturing plants or medical establishments. The degree of discharge from sewage treatment works depends on how they are affected by the treatment process.

1.3. Anaerobic treatment of pharmaceutical wastewater

Effluent from pharmaceutical wastewater normally treated using flocculation, flotation, coagulation, filtration, settling, ion exchange, carbon adsorption, detoxification of active ingredients by oxidation (using ozone wet air oxidation ultraviolet systems or peroxide solutions), and biological treatment (using trickling filters, anaerobic, activated sludge, and rotating biological contactors). Although pharmaceutical wastewater may contain refractory organic materials that cannot be readily degraded, biological treatment is still a viable choice for treatment [22, 23]. However, due to high strength, it is infeasible to treat some pharmaceutical wastewater using aerobic biological processes. Instead an anaerobic process is preferred to remove high-strength organic matter. Recently, the anaerobic treatment of pharmaceutical wastewater containing antibiotics and synthetic drug based effluents has been reported. The detail discussion on this can be found below.

Table–1 shows treatment of various pharmaceutical wastewater using anaerobic processes. Fox and Venkatasubbiah [24] have demonstrated the use of anaerobic baffled reactor (ABR) in the treatment of high sulphate containing pharmaceutical wastewater (Isopropyl Acetate fermentation). These workers found that by inserting a sulphide oxidation unit, the COD removal efficiency could be increased up to 50% at HRT 1 d. Massé *et al.* [25] have explored the effect of antibiotics on psychrophilic anaerobic digestion of swine manure slurry in sequencing batch reactors (SBRs). In their work, six antibiotics, Tylosin, Lyncomycin, Tetracycline, Sulphamethazine, Penicillin and Carbadox, were individually added to a pig diet. It is concluded that only Penicillin and Tetracycline had an inhibitory effect on methane production. Venkata Mohan *et al.* [26] have demonstrated the use of anaerobic suspended film contact reactor (ASFCR) in the treatment of pharmaceutical wastewater from large bulk drug manufacturing unit (aromatic and aliphatic organic chemicals). The organic loading rates were varied from 0.25 to 2.5 kg COD.m⁻³.d⁻¹ and the COD reduction is in the range of 60 to 80% with methane content of around 60 - 70%. Nandy and Kaul [5] demonstrated anaerobic pre-treatment of herbal based pharmaceutical wastewater (e.g. herbs, fruits, flowers, roots, seeds, etc) using fixed-film reactor (FFR) and showed 76 – 98% COD removal at OLR of 10 kg COD.m⁻³.d⁻¹. However, when the OLR increased to 48 kg COD.m⁻³.d⁻¹, the COD removal efficiency dropped to 46 – 50%. They also found that the reactor did not show destabilization under hydraulic and organic shock loadings.

Saravanane *et al.* [27] has demonstrated that a fluidized bed reactor (FBR) under anaerobic conditions could be used to treat anti-osmotic drug based pharmaceutical effluent (Acetic acid and Ammonia). It is reported that COD reduction attained a

maximum value of 88.5% using bioaugmentation through periodic addition of acclimated cells every 2 days with 30 - 73.2 g of cells (1 to 2.5 g.L⁻¹ of reactor volume) from an off-line enricher reactor. Furthermore, they also ventured into studying on bioaugmentation and treatment of Cephalexin drug based pharmaceutical effluent in an up-flow anaerobic fluidized bed (UAFB) system [28]. The results showed that bioaugmentation improved removal efficiency and reactor stability. Ince *et al.* [29] carried out a study on the performance of an up-flow anaerobic filter (UAF) treating a chemical synthesis-based pharmaceutical wastewater (Bacampicilline and Sultamicilline Tosylate) and showed 65% COD removal with methane yield being low at 0.20 m³ CH₄.kg COD_r⁻¹. The performance of a sequencing batch biofilter (SBB) integrating anaerobic-aerobic conditions in one tank to treat a pharmaceutical wastewater (Phenols and O-Nitroaniline) was studied by Buitron *et al.* [30]. The results showed that at HRT 8 - 24 h and OLR of 4.6 - 5.7 kg COD.m⁻³.d⁻¹, a COD removal of 95 - 97% was achieved in the combined system. Anaerobic treatment of pharmaceutical wastewater (Penicillin) containing sulphate (3200 mg.L⁻¹) was carried out by Rodríguez-Martínez *et al.* [31] in an UASB and showed 85 - 90% COD and a sulphate removal of more than 90% were achieved at an OLR of 1.5 kg COD.m⁻³.d⁻¹ and HRT of 8.3 d. However, the performance of the reactor was affected (COD removal dropped to 70%) when the loading rate was increased to 2.09 kg COD.m⁻³.d⁻¹ by reducing the HRT to 7 d. The authors suggested that the accumulation of sulphides could be responsible for the reduced performance. Anaerobic-aerobic treatment of pharmaceutical containing antibiotics (Ampicillin and Aureomycin) was investigated by Zhou *et al.* [32] in an anaerobic baffled reactor (ABR) followed by a biofilm airlift suspension reactor (BASR). The combined system resulted in total COD removal of 97.8% when ABR and BASR were operated at HRT 2.5 d and 12.5 h, respectively. The Ampicillin and Aureomycin removal efficiencies were 42.1% and 31.3% in the ABR, respectively, but did not show substantial removal (less than 10%) in BASR for both antibiotics. More recently, Oktem *et al.* [35] have conducted a study on the performance of a lab-scale hybrid up-flow anaerobic sludge blanket (UASB) reactor, treating a chemical synthesis-based pharmaceutical wastewater. At an OLR of 8 kg COD.m⁻³.d⁻¹, COD reduction of 72% was achieved in the reactor system.

1.3. Treatment of pharmaceutical wastewater-a case study

In this section, a case study of the treatment of pharmaceutical wastewater containing the antibiotic Tylosin in an up-flow anaerobic stage reactor (UASR) is presented. Stage reactors can provide high treatment efficiency for recalcitrant substrates because phase separation, which generates separate environments for acidogenesis and methanogenesis, also promotes favourable conditions for microbial populations involved in the degradation of recalcitrant compounds.

Tylosin is a macrolide antibiotic produced by a strain of *Streptomyces fradiae*. It has good anti-bacterial activity against most pathogenic gram-positive bacteria, and some gram-negative

bacteria, vibrio, spirochete, coccidian, etc. It is one of the first-choice drugs against infections caused by mycoplasma.

[II] MATERIALS AND METHODS

The UASR system [Figure-2] comprise four identical cylindrical Plexiglas compartments (stages), 80 mm internal diameter by 640 mm height, linked in series, was constructed for the present study. The active volume of the UASR system was 11 L (4 stages of 2.75 L). The operational set-up, flow diagram and the reactor design are presented in Figure-2a. Each stage of the reactor had a 3-phase separator baffle, angled at 45° and placed 50 mm below the effluent ports, to prevent floating granules from washing out with the effluent [Figure-2b]. The walls of the reactors were wrapped with a tubular PVC water-jacket, 15mm internal diameter, to maintain the reactor temperature at 37° C. Peristaltic pumps (Watson Marlow 100 series) were used to control the influent feed rate to the first stage of the UASR.

The pharmaceutical wastewater had the following characteristics; soluble COD, 7000 ± 800 mg.L⁻¹; soluble BOD₅, 3500 ± 500 mg.L⁻¹; sulphate, 2500 ± 500 mg.L⁻¹; Total Kjeldahl Nitrogen (TKN), 364 ± 50 mg.L⁻¹; pH, 5.2 - 6.8 and Tylosin concentration, 10 to 220 mg.L⁻¹. In general, this study was carried out in four major steps: 1) start-up of UASR, 2) acclimatisation to pharmaceutical wastewater, 3) increase in OLR (0.43 - 1.86 kg COD.m⁻³.d⁻¹) by altering feed COD (1700 - 7450 mg.L⁻¹) at constant HRT (4 d), and 4) increase in OLR (2.48 - 3.73 kg COD.m⁻³.d⁻¹) by reducing HRT (4 - 2 d) at constant feed COD (7450 mg.L⁻¹). Table-2 shows the reactor operating conditions during investigation of OLR on treatment process. Supernatant liquor, gas and sludge samples were taken separately from each stage for analysis. In addition, gas production rate was determined separately for each stage. Sample analysis included chemical oxygen demand (COD), pH, alkalinity, total Kjeldahl nitrogen (TKN), ammonium nitrogen (NH₃-N), suspended solids (SS), volatile suspended solids (VSS), all according to Standard Methods [39].

Tylosin assay was performed by HPLC on a 20cm Nucleosil C18 analytical column eluted with 60 vols 2 mol.dm⁻³ sodium perchlorate (NaClO₄) and 40 vols of acetonitrile (CH₃CN). Tylosin factors were separated and detected at 280nm. The integrated chromatogram was normalised and the relative percentage of each Tylosin factor reported. Comparison of each Tylosin sample chromatogram with that of a Tylosin base reference standard chromatogram confirmed peak identity for quantification against a 3-point standard curve.

[III] RESULTS AND DISCUSSION

Figure-3 shows temporal changes in the total COD removal and fractional contribution by each stage of the UASR treating pharmaceutical wastewater. Initial fluctuations were attributed to technical problems with the peristaltic feed pump. At a reactor OLR of 1.86 kg COD.m⁻³.d⁻¹ (HRT 4 d), the soluble COD reduction was around 70 - 75%. However, when the OLR was increased to 2.48 kg COD.m⁻³.d⁻¹ (by lowering the HRT, since the strength of the wastewater was limited) the COD removal efficiency decreased gradually until only around 45% soluble COD removal (average removal when reactor approached steady-state) was observed at an OLR of 3.73 kg COD.m⁻³.d⁻¹. It is unlikely that this was caused by limitations in the reactor design as similar ABR have been shown to be capable of over 90% COD removal at OLR of more than 10 kg COD.m⁻³.d⁻¹ [40].

However, pharmaceutical wastewaters containing a high proportion of spent fermentation broths have been shown to require long HRT for efficient treatment [41], presumably on

account of their complex organic carbon content, and this is probably limits the UASR performance at HRT below 4 d.

Table: 1. Anaerobic treatment of pharmaceutical wastewater

Anaerobic Reactor	Type of Pharmaceutical Wastewater	COD Removal (%)	References
Fixed bed	Phenol	93	Bajaj et al [38]
Periodic baffled system	Chinese traditional medicine	34 - 84	Liu et al [37]
Hybrid up-flow sludge bed	Phenol, Dibutyl Phthalate, Bromo Naphthalene, Carbamazepine, Antipyrine	65 - 75	Sreekanth et al [36]
Hybrid up-flow sludge bed	Chemical synthesis	72 – 85	Oktem et al [35]
Up-flow sludge bed	Antibiotic formulation (sulfamerazine)	68 - 89	Sponza and Demirden [34]
Sequencing batch bio-film	Chemical / bulk drugs	51	Venkata Mohan et al [33]
Baffled system	Antibiotic formulation (Ampicillin, Aureomycin)	77 - 90	Zhou et al [32]
Up-flow sludge bed	Antibiotic formulation (Penicillin)	90	Rodriguez-Martinez et al [31]
Sequencing batch	Phenols and O-Nitroaniline	95 - 97	Buitrón et al [30]
Up-flow filter	Chemical synthesis	65	Ince et al [29]
Fluidized bed	Cephalexin drug, anti-osmotic drug	88.5	Saravanane et al [27, 28]
Fixed-film fixed-bed	Herbal-based	76 – 98	Nandy and Kaul [5]
Suspended film contact	Bulk drug (aromatic, aliphatic)	60 – 80	Venkata Mohan et al [26]
Sequencing batch	Swine manure slurry containing antibiotics	80	Massé et al [25]
Baffled system	Isopropyl Acetate	50	Fox and Venkatasubbiah [24]

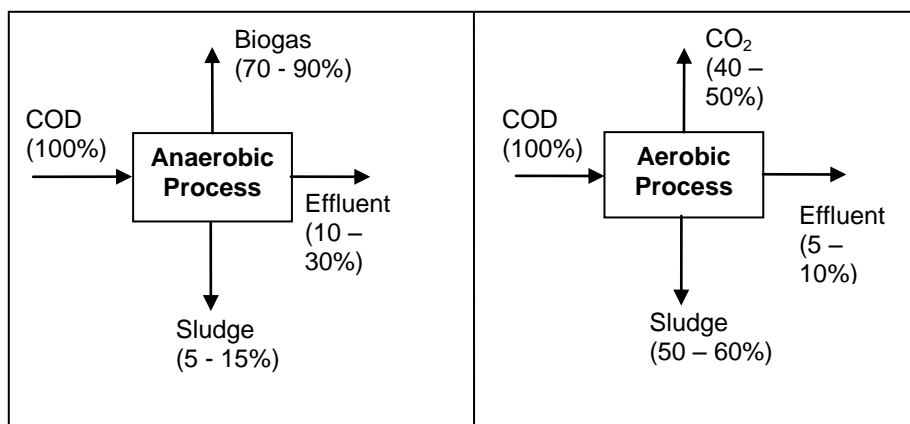


Fig: 1. Advantage of anaerobic system in relation to aerobic treatment [2].

The above results are consistent with observations made by Rodriguez-Martinez *et al.* [31] in an UASB treating pharmaceutical wastewater containing Penicillin G macrolide antibiotics, who found that the COD removal efficiency was 90% at an OLR of 1.5 kg COD.m⁻³.d⁻¹ and HRT 11 d. However, when the OLR was increased to 2.09 kg COD.m⁻³.d⁻¹ by reducing the

HRT to 7 d, the COD removal efficiency dropped dramatically to 70%. They also found that an increase in the OLR resulted in the accumulation of hydrogen sulphide (sulphate in the feed was 3200 mg.L⁻¹) which affected the efficiency of the reactor; the presence of sulphide is known to inhibit the activity of methanogens [42].

Table: 2. Summary of reactor operating conditions during investigation of OLR on treatment process

Brewery (%) [*] wastewater	Pharmaceutical (%) [*] wastewater	Mean OLR (kg COD.m ⁻³ .d ⁻¹)	HRT (d)	Mean Feed COD (mg.L ⁻¹)	Day
50	50	0.43	4.0	1700	1
40-10	60-90	0.86	4.0	3450	41
0	100	1.23	4.0	4900	82
0	100	1.53	4.0	6100	109
0	100	1.86	4.0	7450	166
0	100	2.48	3.0	7450	188
0	100	2.98	2.5	7450	212
0	100	3.73	2.0	7450	231
0	100	1.86	4.0	7450	250

^{*}proportion based on COD

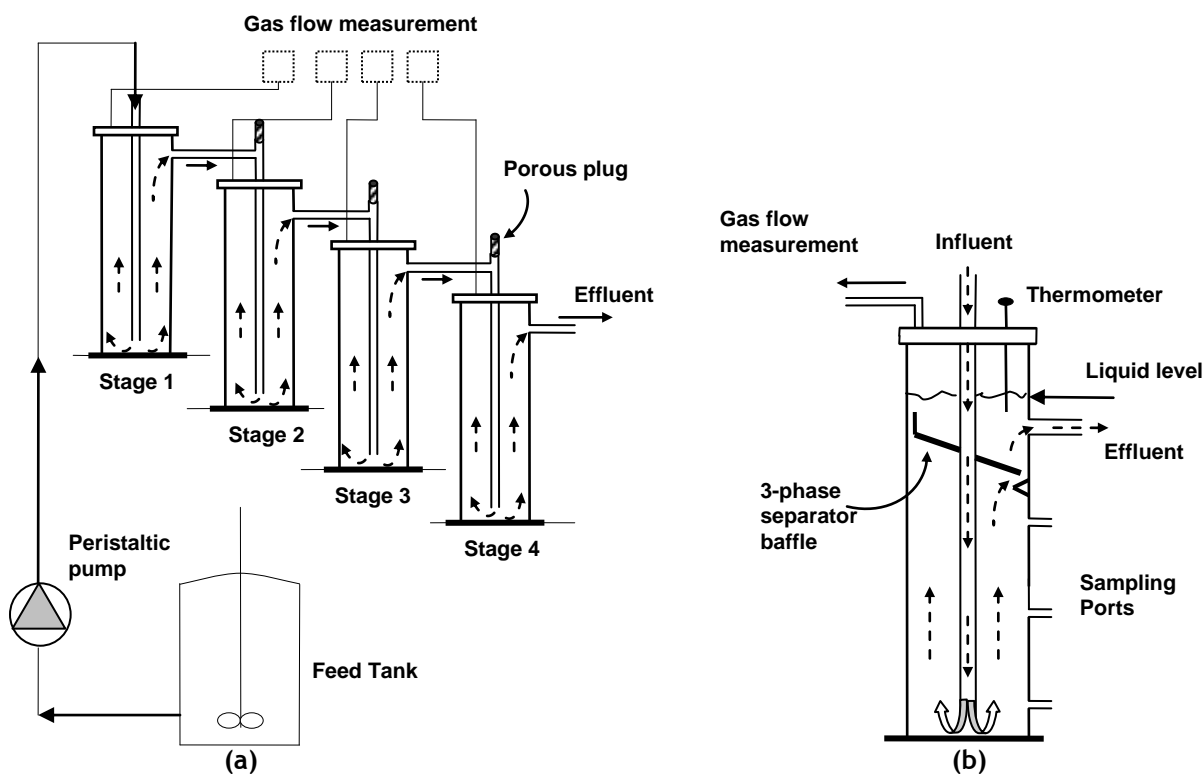


Fig: 2. (a) UASR system and flow regime; (b) details of an individual UASR stage

It is generally known the application of anaerobic treatment process for industrial wastewaters containing high amounts of sulphate has been problematic due to the production of hydrogen sulphide. The presence of H₂S in anaerobic digesters results from the action of sulphate-reducing bacteria (SRB) which utilise sulphate as terminal electron acceptor and compete with acetogens and methanogens for several key substrates in

anaerobic digestion such as propionate, butyrate, ethanol and acetate [43]. Moreover, SRB are generally expected to out-compete other anaerobes in the presence of excess sulphate [44]. The pharmaceutical wastewater used in this study contained high amount of sulphate and sulphide production from this sulphate was thought to be one of the reasons for the poor performance of UASR during the period of high OLR (2.48 – 3.73 kg COD.m⁻³.d⁻¹)

$^3.d^{-1}$). Speece, [45] has stated that at higher OLR, SRB can out-compete with methanogens for substrate since hydrogen sulphide production can be predominant over methane gas production. Kuscü and Sponza, [46] have demonstrated that hydrogen sulphide concentrations in the gas were increased from 160 $mg.L^{-1}$ to 195 $mg.L^{-1}$ when OLR was increased from 2.1 to 3.16

$kg\ COD.m^{-3}.d^{-1}$ in an ABR treating sulphate containing wastewater (*p*-Nitrophenol). Consequently, the decrease in treatment efficiency in the UASR was probably due to sulphide inhibition at higher OLRs (2.48 – 3.73 $kg\ COD.m^{-3}.d^{-1}$).

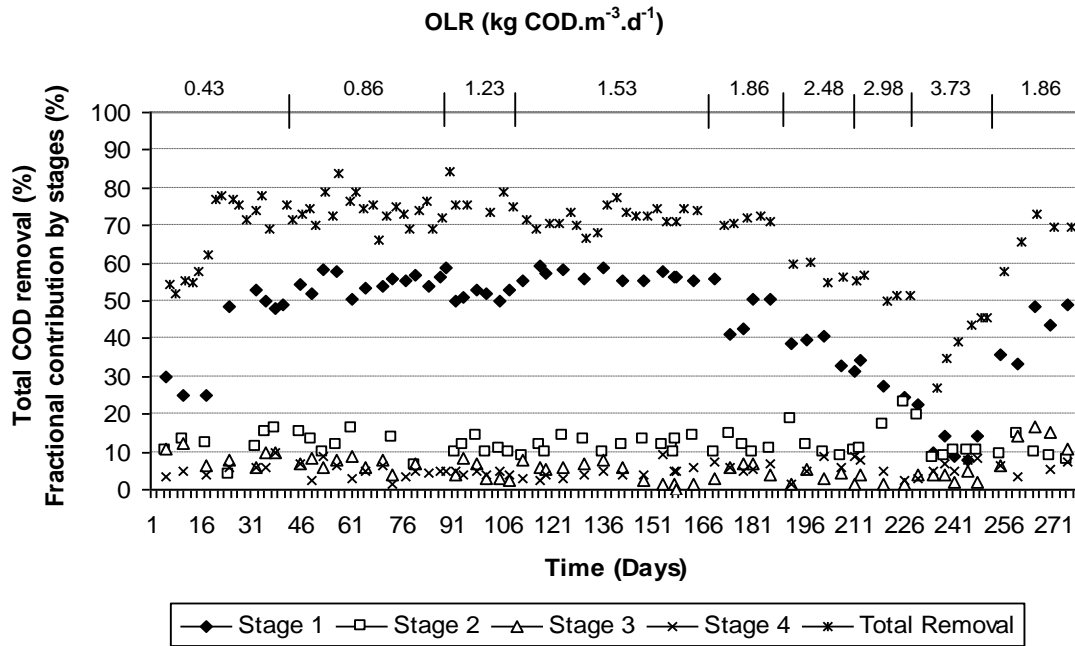


Fig. 3. Total COD reduction (%) of UASR treating pharmaceutical wastewater and fractional contribution (%) to the total COD reduction by each stage at different OLR.

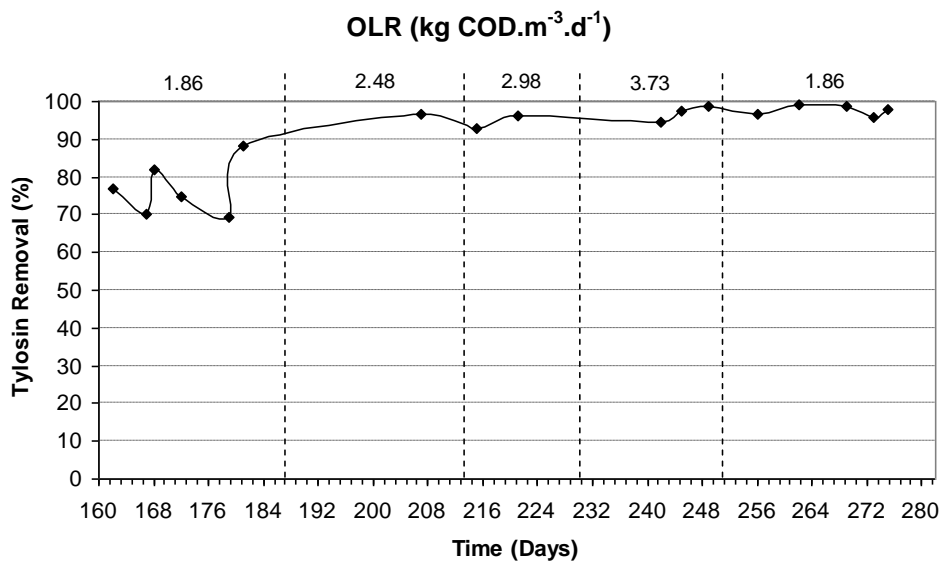


Fig. 4. Antibiotic (Tylosin) reduction profile of UASR at different selected OLR

Fox and Venkatasubbiah [24] reported that as influent pharmaceutical wastewater containing high sulphate was increased to 20% in an ABR, the reactor performance deteriorated (COD removal efficiency reduced from 50 to 20%) as the effluent sulphide concentration increased to inhibitory levels (more than 200 mg.L⁻¹). In addition, Nandy and Kaul [5] have demonstrated that substrate removal efficiency increases with increase in HRT in anaerobic treatment of herbal-based pharmaceutical wastewater using fixed-bed reactor. More recently, Zhou *et al.* [32] reported that when HRT of an ABR treating pharmaceutical wastewater containing antibiotics (Ampicillin and Aureomycin) was extended from 1.25 to 2.5 d, the COD removal efficiency increased from 77 to 85%. They also observed that the antibiotic removal efficiencies increased from 16 to 42% for Ampicillin and 26 to 31% for Aureomycin.

It is evident that stages 2, 3 and 4 showed a relatively minor contribution to total COD removal, around 50 to 60% COD reduction took place in Stage 1 of the UASR when reactor HRT was set to 4 d (i.e. for all reactor OLR at or below 1.86 kg COD.m⁻³.d⁻¹), with less contribution from Stage 2 (around 10 - 15%), and Stage 3 and 4 accounting for around 5%. This also suggests that it was the physiological characteristics of the Stage 1 effluent that limited further COD degradation in subsequent stages of the reactor, rather than excessive OLR, although as the pH was reduced in all stages at the highest OLR (data not presented), there is a possibility that the methanogenic biomass in Stages 2, 3 and 4 could also have been affected adversely by the acidic conditions generated in Stage 1. Another possible reason could be the sulphide toxicity at higher OLRs in Stage 1 which inhibited the methanogens in Stage 2, 3 and 4. Moreover, the increase in OLR (by decreasing in HRT) had a greater adverse effect on COD degradation efficiency than increases in substrate concentration at a fixed HRT. In UASR, the decrease in HRT decreased treatment efficiency, especially in Stage 1, and since other stages were not working effectively, the overall treatment efficiency is low.

In this study, Tylosin concentration in the pharmaceutical wastewater feed varied from 10 to 220 mg.L⁻¹ and Figure 4 shows the Tylosin degradation profile throughout the experimental study in the UASR. Tylosin removal efficiency fluctuated from 70 - 88% at OLR 1.86 kg COD.m⁻³.d⁻¹, however, the removal efficiency remained relatively constant (93 - 99%) at OLR 2.48 - 3.73 kg COD.m⁻³.d⁻¹. Similar removal trend was also observed when the reactor OLR was reduced to 1.86 kg COD m⁻³ d⁻¹ [Figure-4], with an average Tylosin concentration in the treated wastewater of 3 mg.L⁻¹ for the all OLR investigated. This confirms that Tylosin was readily degraded in the reactor under anaerobic conditions. In contrast to the COD removal profile, which showed reducing COD removal efficiency with increasing OLR, Tylosin concentration remained relatively constant in the reactor effluent throughout the experiment. These results are consistent with the view that typical wastewater concentrations of Tylosin have a relatively minor influence on the overall COD removal efficiency of UASR and do not inhibit substantially the activity of methanogenic populations. Some may argue Tylosin is hardly biodegradable

and could contribute to high COD in the effluent; however, we believe, the anaerobic treatment system (UASR) operated to efficiently remove most of the general COD associated with fermentation waste residues in the real pharmaceutical wastewater containing Tylosin. Further polishing by aerobic degradation would be viable if tight discharge consent applied (i.e. aerobic polishing after anaerobic digestion process is better than using aerobic to degrade all COD).

[IV] CONCLUSIONS

Anaerobic treatment system is a promising alternative for pharmaceutical wastewater treatment. Results from the existing treatment of pharmaceutical wastewater using anaerobic system demonstrates that anaerobic treatment is suitable for treating various type of pharmaceutical wastewater. The application of anaerobic digestion to recalcitrant streams such as those from pharmaceutical production would provide significant environmental and economic benefits to pharmaceutical industry. The UASR system is an appropriate option for pre-treatment of wastewaters with a highly complex organic composition, such as pharmaceutical wastewater. Results of this study suggest that at a reactor OLR of 1.86 kg COD.m⁻³.d⁻¹ (HRT 4 d); the soluble COD reduction was around 70 - 75%. Under these conditions, an average of 95% Tylosin reduction was achieved in the, indicated that this antibiotic could be degraded efficiently in the anaerobic reactor system. However, when the OLR was increased to 2.48 - 3.73 kg COD.m⁻³.d⁻¹, by lowering the HRT, the COD removal efficiency decreased to 45%. Whilst COD degradation efficiency might be affected by the complexity and variability of the real pharmaceutical wastewater, long HRT in the UASR can lessen these effects.

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