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Treatment of Selected Pharmaceutical Drugs in a Batch Aerobic Suspended-growth Bioreactor

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Contents

Introduction

- Pharmaceutical drugs are produced in large quantities worldwide and find their way in wastewaters generated from households, hospitals and the pharmaceutical industry.
- Five different commonly used drugs, namely metronidazole, trimethoprim, sulphamethoxazole, paracetamol, and ranitidine, were considered in this study since they are found at different concentrations in most of the wastewaters generated from various sources.
- According to characterization studies of wastewaters from different sources, the concentration of these drugs in wastewaters may vary from 0.1 to 10 mg/L, with the lower values found in domestic wastewaters and the higher values observed in factory effluents from pharmaceutical industries.

Characteristics of Drugs

Metronidazole $C_6H_9N_3O_3$ → marketed under the brand name Flagyl among others, it is an antibiotic and antiprotozoal medication.

Trimethoprim $C_{14}H_{18}N_4O_3$ → an antibiotic used mainly in the treatment of bladder infections.

Sulphamethoxazole $C_{10}H_{11}N_3O_3S$ → an antibiotic used for bacterial infections such as urinary tract infections, bronchitis, and prostatitis.

Paracetamol $C_8H_9NO_2$ → also known as acetaminophen, is a medication used to treat pain and fever.

Ranitidine $C_{13}H_{22}N_4O_3S$ → sold under the trade name Zantac among others, is a medication that decreases stomach acid production.

Laboratory Experiments

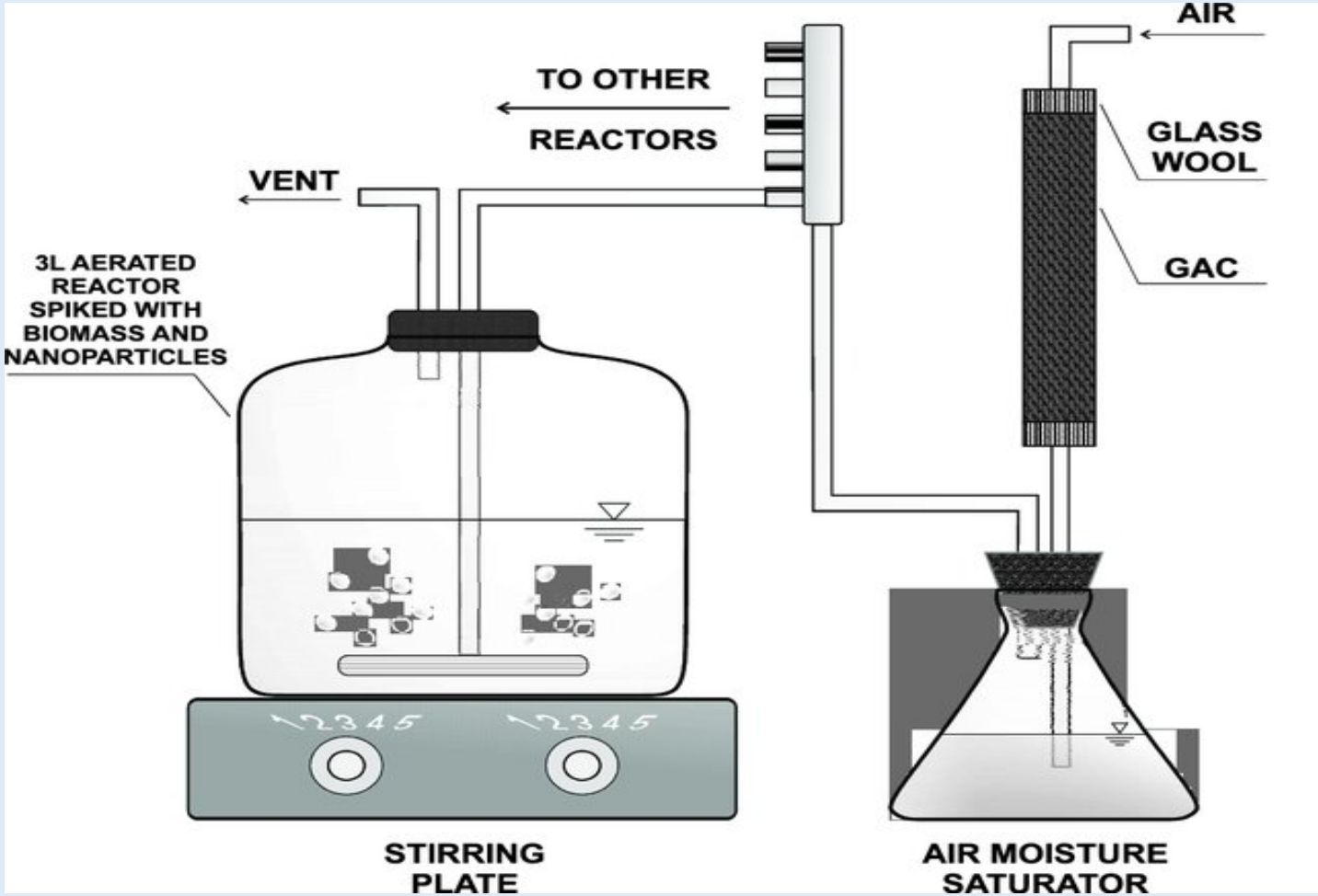
Drugs

- **Metronidazole**: $C_6H_9N_3O_3$
- **Trimethoprim**: $C_{14}H_{18}N_4O_3$
- **Sulphamethoxazole**: $C_{10}H_{11}N_3O_3S$
- **Paracetamol**: $C_8H_9NO_2$
- **Ranitidine**: $C_{13}H_{22}N_4O_3S$

- **Wastewater TOC 300 mg/L (Shimadzu TOC analyzer)**
- **Spiked Drug Concentrations: 0.1, 1.0, 10 mg/L (HPLC)**
- **5 batch reactors, each 3 L**
- **MLSS = 2500 mg/L**
- **pH = 6.8, T = 25 °C , Air Flow = 96 mg/L, DO 2.5 mg/L**

Experimental Conditions

- Analytical grade chemical nutrients as well as pharmaceutical drugs were used to prepare synthetic wastewater samples spiked with drugs at preset experimental conditions. The chemicals were dissolved in distilled water. The synthetic wastewater used in this study had an initial TOC of about 350 mg / L.
- The batch tests were conducted in glass containers (reactors) of 3 L liquid-capacity each. A total of 5 reactors each spiked with one of the drugs as well as a control reactor were operated in the laboratory at room temperature (20 ± 1 ^{o}C) .
- The experimental set-up is shown in the following figure.



Laboratory experimental set-up

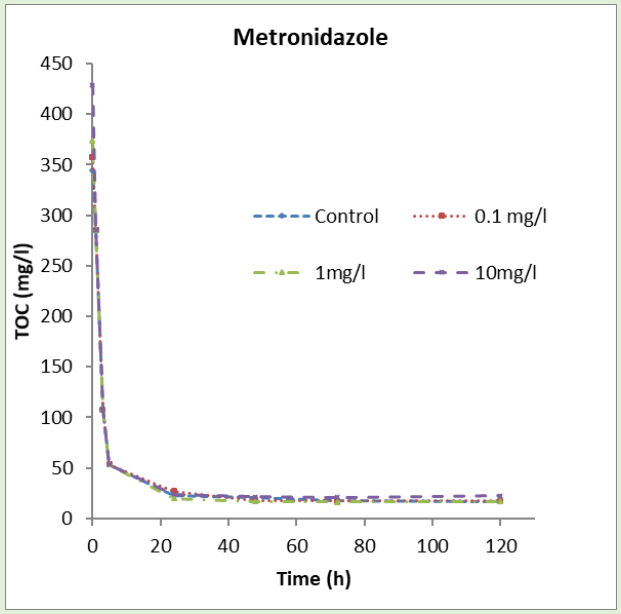
Experimental Program

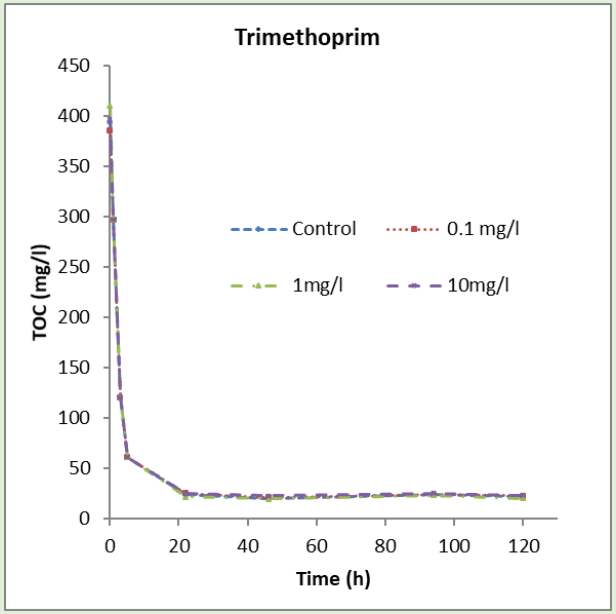
- Effect of Aeration time
- Effect of drug concentration
- Kinetic analysis of organic reduction
- Changes in pH during operation
- Growth of Biomass (MLSS)

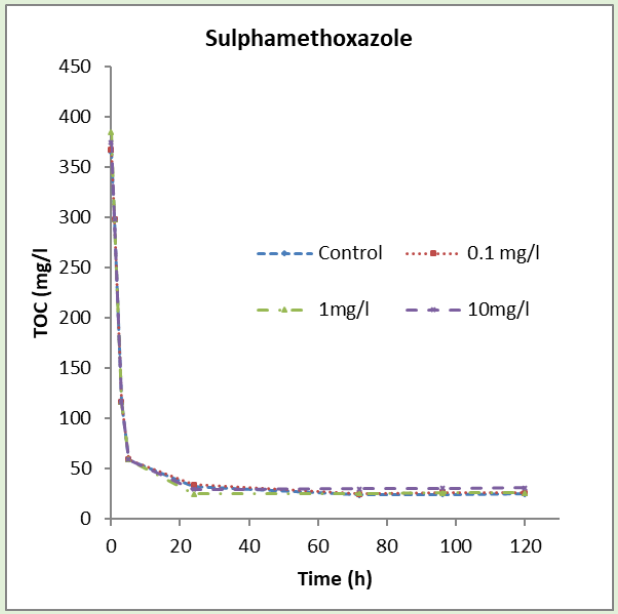
→ Statistical Analysis of Data

Analysis of Variance (ANOVA) Test

Effect of Time on TOC Reduction for Different Drug Concentrations







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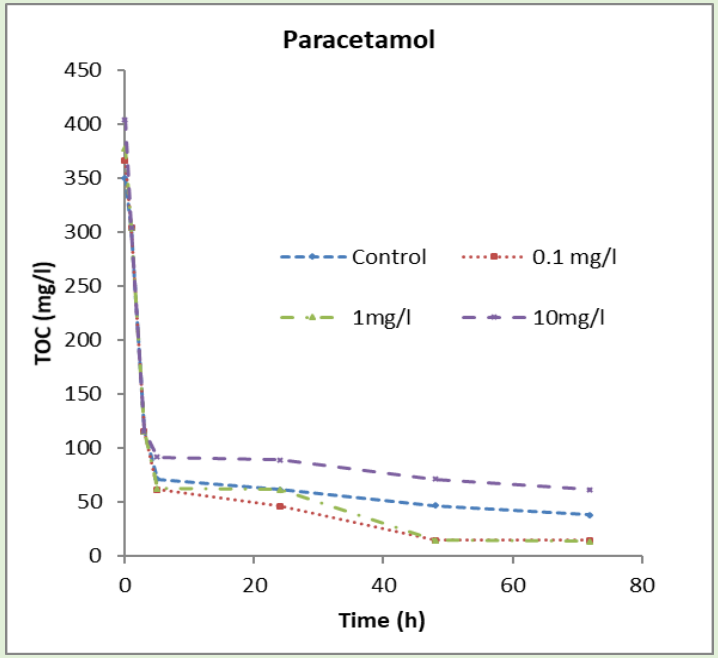
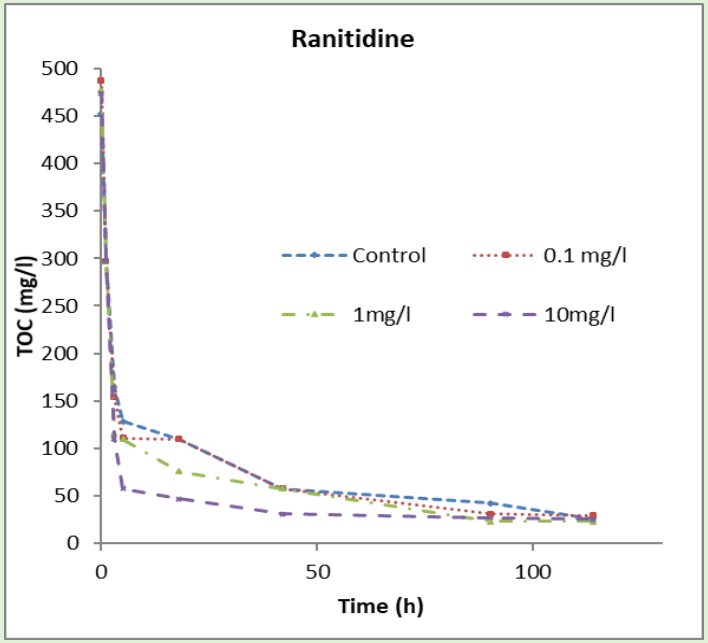


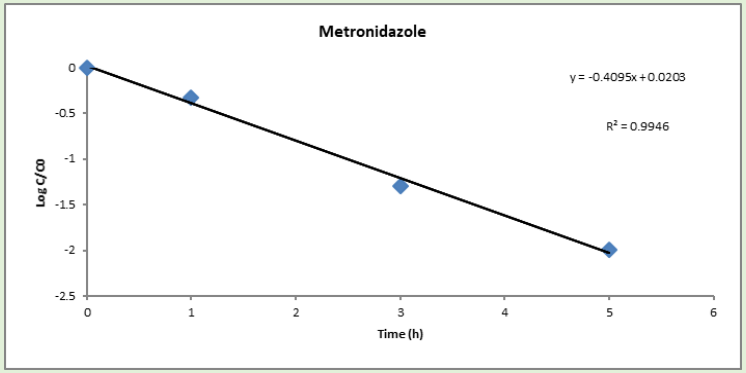


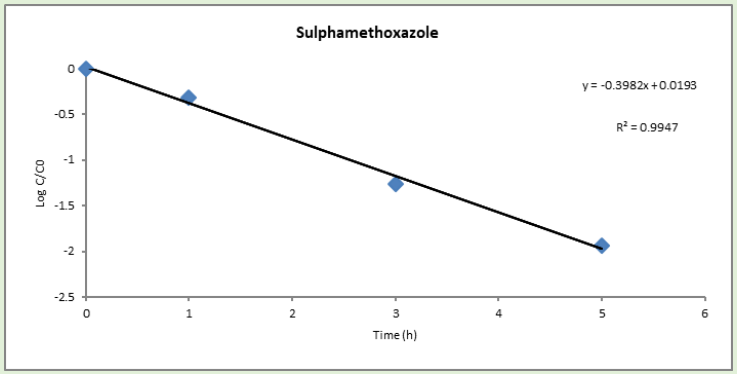
Kinetic Model

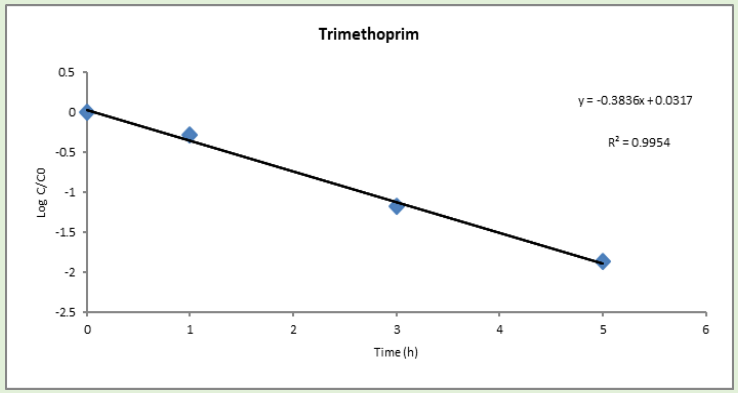
- $dC/dt = -kC$ (1)
- $\frac{C}{C_0} = e^{-kt}$ (2)
- C_0 = initial substrate concentration (mg/L)
- C = substrate concentration at any time t (mg/L)
- t = time (h) , K = degradation rate constant (h-1)

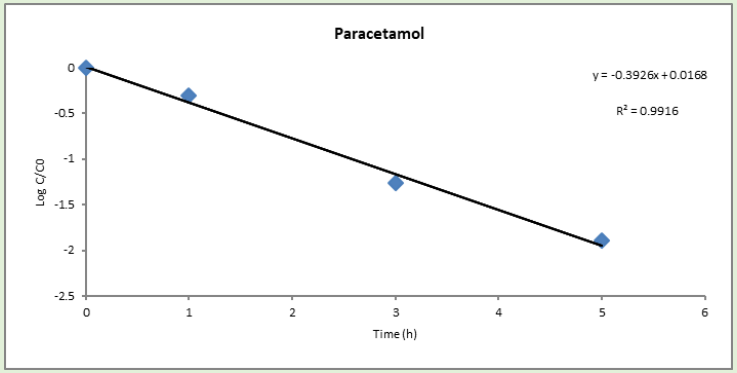
- No inhibitory effects
- Pseudo first-order kinetic model
- Effect of drug concentration

Kinetic plots of TOC reduction during batch experiments





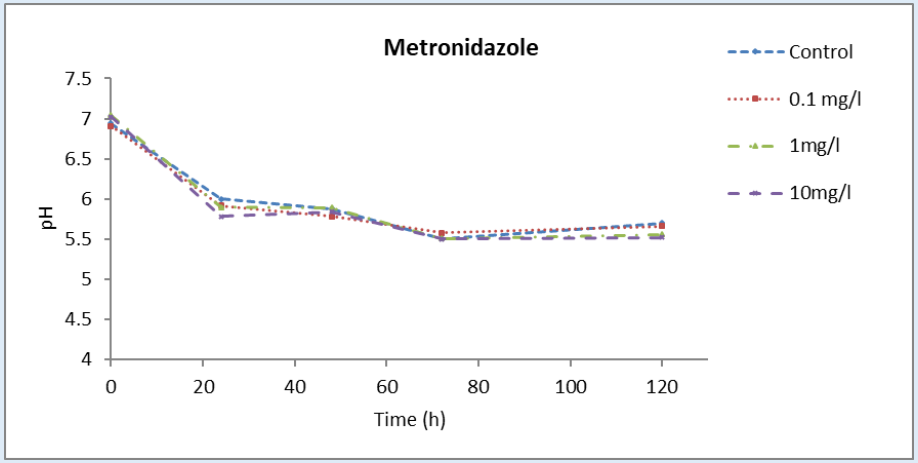


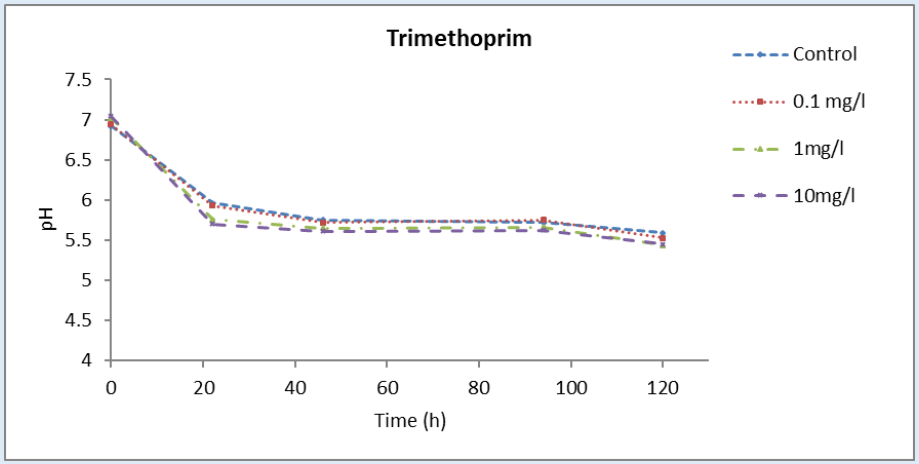


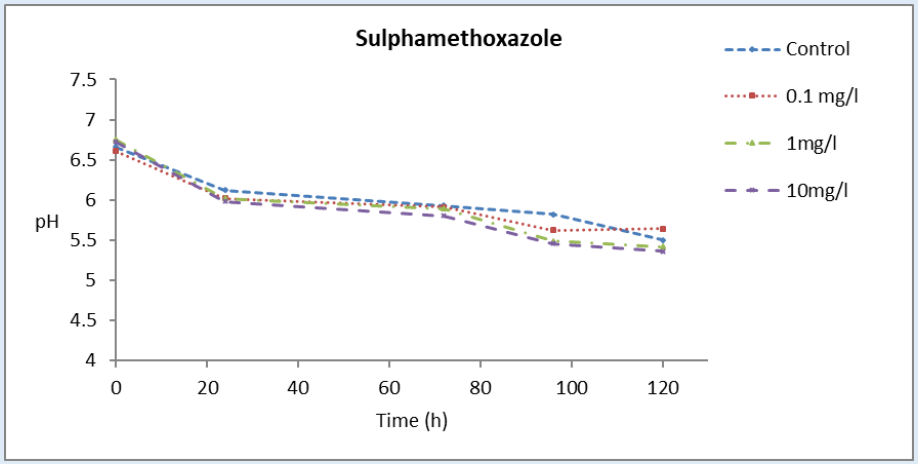
Kinetic analysis of organic reduction at different drug concentrations

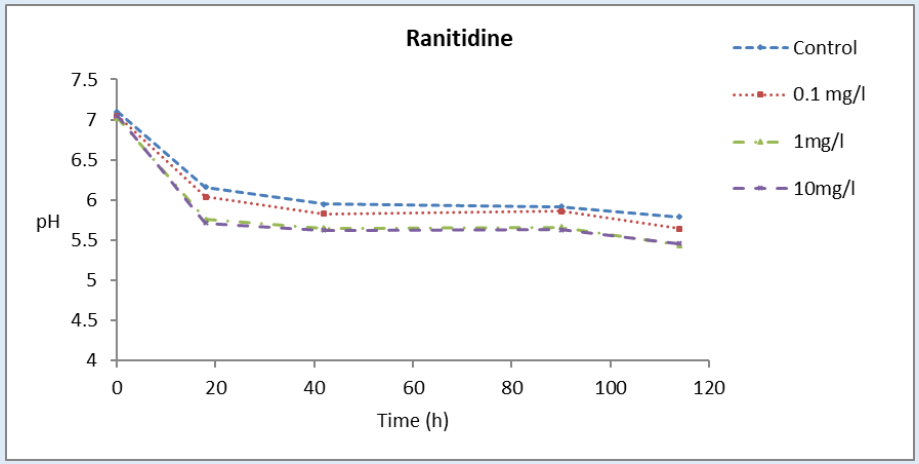
Drug	concentration	0 hour	24 hour	96 hour	K	R^2	% Drug Removal
Metronidazole $C_6H_9N_3O_3$	0.1 mg/l	0.1 (±0.0117)	0.038 (±0.00448)	0.0226697 (±0.00266)	0.669	0.667	77.33
	1 mg/l	1 (±0.003)	0.67 (±0.002)	0.336 (±0.001)	0.639	0.925	66.37
	10 mg/l	10 (±0.07)	8.277 (±0.06)	1.931 (±0.014)	0.85	0.998	80.68
Trimethoprim $C_{14}H_{18}N_4O_3$	0.1 mg/l	0.1 (±0.0014)	0.06179 (±0.00088)	0.00985 (±0.00014)	0.888	0.963	90.149
	1 mg/l	1 (±0.0768)	0.34939 (±0.0268)	0.09415 (±0.007)	0.807	0.746	90.585
	10 mg/l	10 (±0.014)	9.122618 (±0.013)	0.749432 (±0.001)	1.009	0.975	92.505
Sulphamethoxazole $C_{10}H_{11}N_3O_3S$	0.1 mg/l	0.1	0 (±0)	0 (±0)	0.803	0.486	100
	1 mg/l	1 (±0.2)	0.544384 (±0.11)	0.029109 (±0.0058)	0.943	0.94	97
	10 mg/l	10 (±0.2)	7.676293 (±0.15)	0.435618 (±0.0087)	0.998	0.999	95.64
Paracetamol $C_8H_9NO_2$	0.1 mg/l	0.1 (±0.002)	0 (±0)	0 (±0)	4.166	1	100
	1 mg/l	1 (±0.02)	0 (±0)	0 (±0)	4.166	1	100
	10 mg/l	10 (±1.5)	0 (±0)	0 (±0)	4.166	1	100
Ranitidine $C_{13}H_{22}N_4O_3S$	0.1 mg/l	0.1 (±0.002)	0.003687 (±0.0003)	0 (±0)	0.813	0.513	100
	1 mg/l	1 (±0.16)	0.119911 (±0.019)	0.043215 (±0.007)	0.791	0.552	95.678

Changes in pH during operation of batch reactors

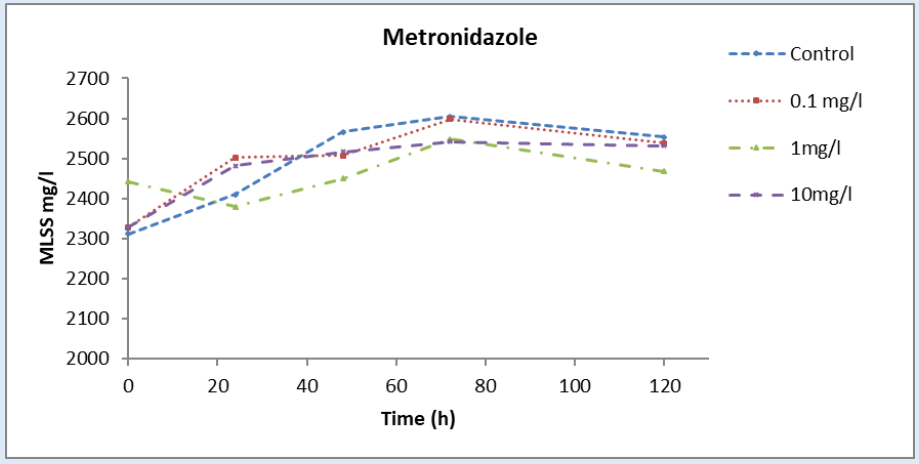


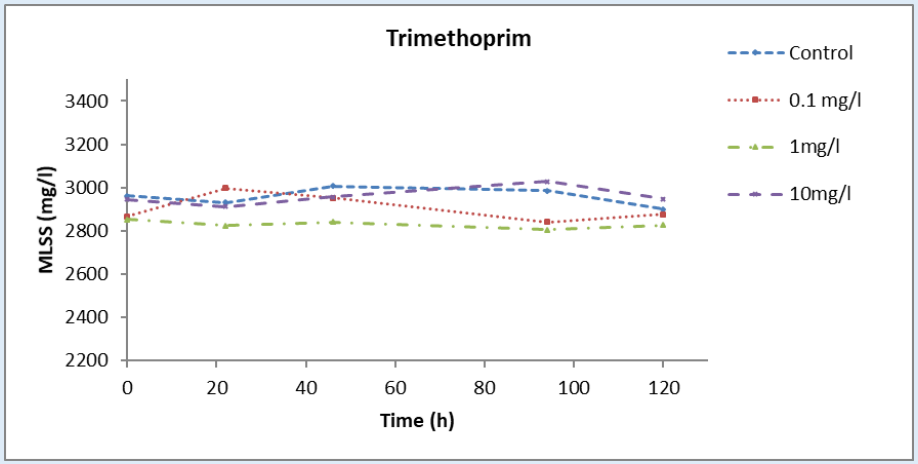


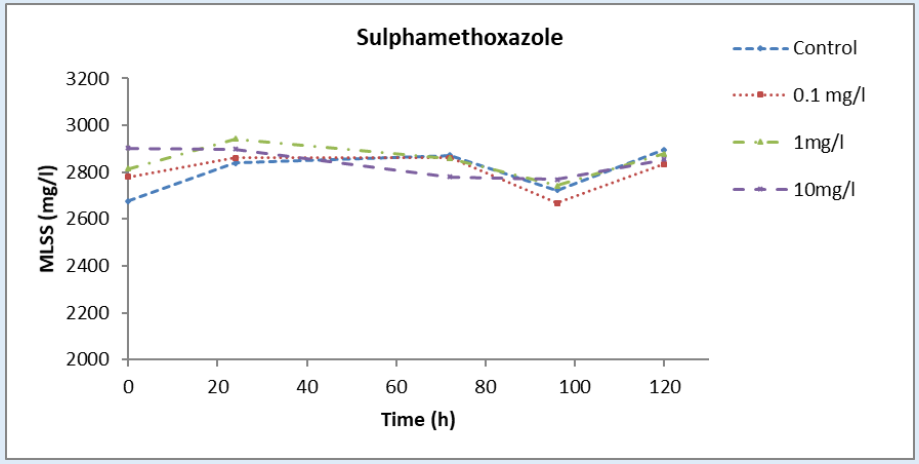


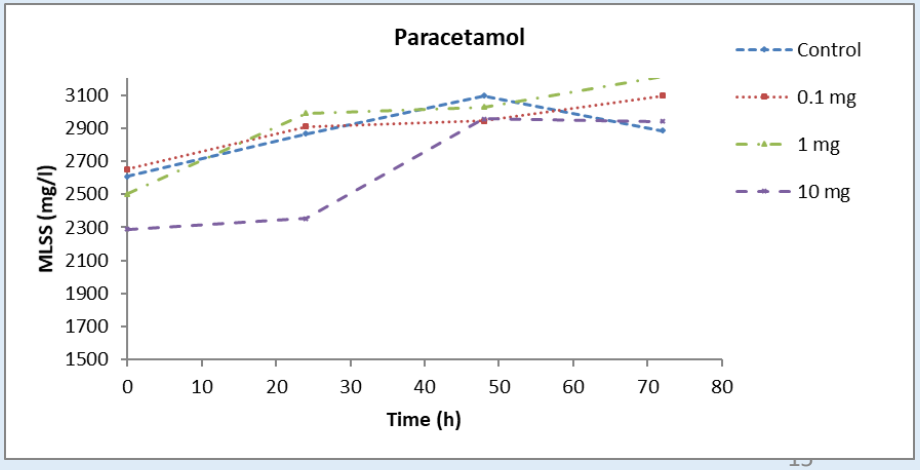


Change in MLSS during operation of batch reactors.









		Toc % Removal	Biodegradation rate TOC mg/mg day	MLSS (K)	Drug % Removal	Drug degradation rate mg/mg day
Metronidazole $C_6H_9N_3O_3$	p-value	0	0.324	0.48	0	0.307
	Confidence level (1 - p-value)*100]	100	67.6	52	100	0.693
	Level of Significance	Highly Significant	Insignificant	Insignificant	Highly Significant	Insignificant
Trimethoprim $C_{14}H_{18}N_4O_3$	p-value	0	0.322	0.294	0	0.307
	Confidence level (1 - p-value)*100]	100	67.8	70.6	100	0.693
	Level of Significance	Highly Significant	Insignificant	Insignificant	Highly Significant	Insignificant
Sulphamethoxazole $C_{10}H_{11}N_3O_3S$	p-value	0	0.321	0.341	0	0.307
	Confidence level (1 - p-value)*100]	100	67.9	65.9	100	69.3
	Level of Significance	Highly Significant	Insignificant	Insignificant	Highly Significant	Insignificant
Paracetamol $C_8H_9NO_2$	p-value	0	0.321	0.25	0	0.307
	Confidence level (1 - p-value)*100]	100	67.9	75	100	69.3
	Level of Significance	Highly Significant	Insignificant	Insignificant	Highly Significant	Insignificant
Ranitidine $C_{13}H_{22}N_4O_3S$	p-value	0	0.325	0.11	0	0.307
	Confidence level (1 - p-value)*100]	100	67.5	89	100	69.3
	Level of Significance	Highly Significant	Insignificant	Less Significant	Highly Significant	Insignificant

Conclusions

1. High removal efficiencies were obtained for organics based on a gross parameter such as TOC or specific drug reduction, with efficiencies up to 95% and 90% obtained , respectively. Paracetamol showed the highest removal efficiency among the five selected drugs.

2. All the drugs tested proved to be biodegradable at the concentration levels studied and did not exhibit inhibitory effects influencing normal process operation over a wide range of drug concentrations found in domestic, medical and pharmaceutical factory wastewaters.

2. A pseudo first-order degradation kinetic model was followed using all five drugs at all the concentration levels studied. The removal rates can be predicted using such a model since high correlation coefficients were obtained as the data were fitted to the model.

3. The drug removal rates increased as the drug concentration was increased. Therefore, dilution of wastewater (e.g. by extraneous water) is not needed as it may reduce the degree of biological removal.

4. Statistical analysis using the ANOVA test revealed that the initial drug concentration has a significant effect on removal and biodegradation of the drug in the concentration range studied from 0.1 to 10 mg/L.

Thank you

Questions ?