EFFECT OF ANTIMICROBIAL DISCHARGES INTO WASTEWATER TREATMENT PLANTS IN THE PHARMACEUTICAL INDUSTRY

by

Manisha Y. Gunasekera

Dissertation submitted to the Department of Civil Engineering
University of Moratuwa
Sri Lanka

for the partial fulfillment of

Master of Engineering in Environmental Engineering and Management

November 1998

This dissertation has not been previously prepared in whole or part to any University or Institution for a Higher Degree.

M. Y. Gunasekera

(Manisha Y. Gunasekera)

November 1998

Acknowledgement

I acknowledge with gratitude the Chairman and the Management of State Pharmaceuticals Manufacturing Corporation, in giving me the opportunity to carryout this project at their Production facility at Ratmalana.

I am grateful to Dr (Mrs.) Indrika Abeyagunawardane and Dr.Ajith De Alwis, my co-supervisors whom very generously spared their precious time and provided every guidance and assistance to carry out this difficult task.

I extend my gratitude and thanks to Prof. (Mrs.) N.Ratnayaka, Head Environmental Engineering Division, Civil Engineering Department, University of Moratuwa and Dr. (Mrs.) Indrika Abeyagunawardena, Head, Department of Microbiology, University of Kelaniya for providing me with all necessary assistance in carrying out the analysis.

I am also thankful to the members of staff at SPMC, Microbiology Department University of Kelaniya and Environmental Engineering Division, Civil Engineering Department, University of Moratuwa for the assistance extended to me.

Summary

Pharmaceutical manufacturing industry is expected to generate effluents having a wide variety of antimicrobial substances. The biological wastewater treatment processes should thus be capable of handling effluents, containing these inhibitory materials, without being adversely affected.

In this investigation, the study of the wastewater treatment system of a Pharmaceutical Manufacturing facility is carried out with special reference to antimicrobial discharges. The manufacturing process studied dealt with formulation, filling and packaging of preparation for prescription products. Thus this facility falls into the `dry formulation' category. A good clean supply of water is essential in this industry. The water used in the manufacturing areas is mainly for cleaning/washing of processing equipment and accessories. Water is also used for cooling the housing of the moving parts in machines. All liquid effluents generated pass through a wastewater treatment plant prior to discharge into an inland surface water body.

The wastewater treatment plant in this facility consists of an activated sludge treatment process. For a primary understanding of this wastewater treatment plant a study of the general characteristics were done. The effect on the overall efficiency of the wastewater treatment plant was observed while studying the washing/cleaning activities carried out in the production zones on each sample collecting day. The findings of this study showed an overall efficiency less than the design efficiency of the wastewater treatment plant. It is seen that plant inputs and generated waste loads are low even when compared with typical waste characteristics of such facilities. A large fraction of the BOD/COD ratios determined showed low values. About 92% of the BOD/COD ratios determined in the equalization tank were less than 0.5. The analysis of BOD, with different dilutions was done in order to determine whether there is an effect by any antimicrobial substance on the biological activity.

The BOD test carried out for a series of wastewater sample dilutions showed decreasing BOD values as the dilution percentage increasing on certain days. In some days results showed 31% to 34% reduction in BOD value indicating the presence of an antimicrobial substance in the wastewater sample on that day.

Further, in order to study the antimicrobial activity of the wastewater discharged from this facility, *E. coli* was tested in liquid culture medium. The growth of *E. coli* was monitored as absorbance at 600nm in the presence and absence of waste samples.

The results indicated the growth of *E. coli* in wastewater was not as high as the growth shown in the peptone water medium. It was also indicated that the growth of this organism in the wastewater sample was not inhibitory as in the solution containing amoxycillin (10μg/ml).

A study of the effect on the same organism was also carried out using the antibiotic diffusion technique. The inhibition zones created from a concentration series of an antimicrobial substance were studied with the inhibition zone produced by wastewater.

The study carried out using the cylinder plate test showed an inhibition zone for wastewater. For a wastewater sample taken from the wastewater treatment plant after cleaning Rifampicin processed machines, a clear zone was observed giving an effect equivalent to a concentration of 2.9 μg of amoxycillin per milliliter.

From the observed results, heavy impact on the wastewater treatment plant operation from discharges was not indicated. However the precautions are needed to be taken when contemplating expansion etc. as the present observations and conclusions apply only to current loading conditions. Close monitor of waste effluent would be necessary in future if expansion is sought by the company.

Table of Contents

Chapter 3

State Pharmaceuticals Manufacturing Corporation Production Facility and its Wastewater Treatment Plant

Chapter 4

Study of General Characteristics of the Wastewater Treatment Plant

Chapter 5

Antimicrobial Effect Study

Chapter 6

Chapter 7

Conclusions and Suggestions for Further Study

References

Appendices

List of Figures

List of Tables

List of Abbreviations

BAT	Best Available Technology
BATNEEC	Best Available Technology Not Entailing Excessive Cost
BBT	Bacterial Bioluminescence Test
BOD	Biochemical Oxygen Demand
BP	British Pharmacopoeia
CFU	Colony Forming Units
COD	Chemical Oxygen Demand
DO	Dissolved Oxygen
EPA	Environmental Protection Agency
F/M	Food to Microorganism
GAC	Granular Activated Carbon
GD	General Drugs
GMP	Good Manufacturing Practices
MLSS	Mixed Liquor Suspended Solids
N/A	Not Applicable
NA	Nutrient Agar
NTU	Nephelometric Turbidity Units
OUR	Oxygen Uptake Rate
PCA	Plate Count Agar
R&D	Research and Development
SBL	Still Base Liquor
SIC	Standard Industrial Classification
SPC	State Pharmaceutical Corporation
SPMC	State Pharmaceutical Manufacturing Corporation
SS	Suspended Solids
TS	Total Solids
TSS	Total Suspended Solids
USP	United States Pharmacopoeia
UV	Ultra Violet
WHO	World Health Organization
WWTP	Wastewater Treatment Plant