ANTIBACTERIAL ACTIVITY OF COMMONLY PRESCRIBED ALLOPATHIC MEDICINES AGAINST DIFFERENT BACTERIAL STRAINS

Project Work By

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CERTIFICATE

This is to certify that the project report entitled "**ANTIBACTERIAL ACTIVITY OF COMMONLY PRESCRIBED ALLOPATHIC MEDICINES AGAINST DIFFERENT BACTERIAL STRAINS**" submitted by **Ms. Riya Tresa Binoy, Reg. No. AB20ZOO009** in partial fulfilment of the requirement of Bachelor of Science degree in Zoology of Mahatma Gandhi University, Kottayam is a bonafide work done under my guidance and supervision and to the best of my knowledge, this is her original effort.

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EXAMINERS:

1)

2)

DECLARATION

I, Ms. RIYA TRESA BINOY, hereby declare that this project report entitled "ANTIBACTERIAL ACTIVITY OF COMMONLY PRESCRIBED ALLOPATHIC MEDICINES AGAINST DIFFERENT BACTERIAL STRAINS" is a bonafide record of work done by me during the academic year 2022-2023 in partial fulfilment of the requirements for Bachelor of Science degree in Zoology of Mahatma Gandhi University, Kottayam.

This work has not been undertaken or submitted elsewhere in connection with any other academic course and the opinions furnished in this report are entirely my own.

RIYA TRESA BINOY

REG NO.: AB20ZOO009 SIGNATURE

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TABLE OF CONTENTS

ABSTRACT

The project entitled – "Antibacterial Activity of Commonly Prescribed Allopathic Medicines against Different Bacterial Strains" tested the antibacterial efficacy of azithromycin, amoxicillin, cefixime, cefpodoxime, norfloxacin and ofloxacin on 3 Gram-negative (*Escherichia coli, Klebsiella, Vibrio parahaemolyticus*) and 3 Gram-positive (*Enterococcus, Staphylococcus aureus, Streptococcus iniae*) bacteria. The antibacterial effect was measured using Kirby-Bauer disc diffusion method. From the study, it was found that ofloxacin was the most effective medicine while amoxicillin was the least effective against the bacteria studied. It was also observed that medicines prescribed for respiratory ailments showed greater activity against enteric bacteria. The most sensitive bacteria were *Klebsiella* (found in the respiratory and intestinal tract) and *Enterococcus* (enteric bacteria) while the least sensitive bacteria was *Vibrio parahaemolyticus* (enteric bacteria).

INTRODUCTION

Bacteria are single-celled microorganisms that lack a nuclear membrane and are metabolically active (Baron S., 1996). They are a major source of infections around the world. A method of treatment of these infections is using allopathic medicines. Though allopathy has various definitions, in the present study it is used to describe conventional modern medicines that treat symptoms and diseases based on evidence obtained from extensive research. It is also known as mainstream medicine, orthodox medicine and Western medicine. The term allopathy is in common use in India to differentiate Western medicines from the other systems of medicine found there including Ayurveda and homeopathy.

In allopathy, antibiotics are prescribed based on the type and seriousness of the infection present in an individual (Werth, 2022). In many cases, the species of bacteria determine the antibiotic prescribed. Antibiotics have been widely accessible to the public since the 1940s (Fisher, 2006). Due to their widespread use, many bacterial species have developed resistance to commonly used antibiotics. Therefore, new antibiotics need to be formulated on a regular basis to keep up with the ability of bacteria to develop resistant strains over time.

The respiratory tract and the gastrointestinal tract are common sites for bacterial infections. The decreasing efficacy of antibiotics in common use has led to the idea of examining their effectiveness against bacteria other than the ones they are typically prescribed for.

The present study aims to analyse the antibacterial effect of some commonly prescribed antibiotics (azithromycin, amoxicillin, cefixime, cefpodoxime, norfloxacin, ofloxacin) against various Gram-negative (*Escherichia coli, Klebsiella, Vibrio parahaemolyticus*) and Gram-positive (*Enterococcus, Staphylococcus aureus, Streptococcus iniae*) bacteria that cause intestinal and respiratory ailments.

AZITHROMYCIN

Azithromycin is an antibiotic commonly prescribed for respiratory infections, chest infections and dental abscesses. It is a macrolide antibacterial drug. Each millilitre of the medicine contains Azithromycin IP equivalent to Azithromycin anhydrous 20 mg.

AMOXICILLIN

Amoxicillin is a penicillin antibiotic. It is used to treat various respiratory ailments including chest infections and pneumonia. Each 5 ml contains Amoxicillin trihydrate IP equivalent to Amoxicillin 250 mg.

CEFIXIME

Cefixime is a broad-spectrum antibiotic. It is a cephalosporin that is commonly prescribed for bronchitis, gonorrhoea and infections of the ears, throat, tonsils and urinary tract. Each 5 ml contains Cefixime IP as trihydrate equivalent to anhydrous Cefixime 50 mg.

CEFPODOXIME

Cefpodoxime is used to treat bronchitis, pneumonia, gonorrhoea and infections of the skin, ear, sinuses, throat, tonsils and urinary tract. It is also a cephalosporin. Each 5 ml contains Cefpodoxime proxetil IP equivalent to Cefpodoxime 100 mg.

NORFLOXACIN

Norfloxacin is a member of the antibiotic class fluroquinolone. It is prescribed to treat various bacterial infections of the urinary tract and intestine. Each tablet contains Norfloxacin IP 400 mg.

OFLOXACIN

Ofloxacin is a broad-spectrum antibiotic. It is used to treat certain infections of the skin, upper respiratory tract and urinary tract. It is a fluroquinolone. Each tablet contains Ofloxacin IP 200 mg.

REVIEW OF LITERATURE

Antibiotics are medicines used to treat and prevent bacterial infections. The bacteriostatic or bactericidal abilities of antibiotics have made them effective choices against various bacteria. Antibiotics function by blocking the vital processes of the bacteria therefore preventing it from undergoing replication and forming new copies.

Since the discovery of penicillin in 1928, which sparked the golden age of antibiotic discovery, these medicines have been popular choices for the treatment of bacterial infections. The constant use of antibiotics has led to the rise of many antibiotic-resistant strains of bacteria. These strains are known to be resistant towards most of the discovered antibiotics therefore the need for the innovation and discovery of new antibiotics has become imperative. The effectiveness of antibiotics against bacteria other than the ones they are commonly prescribed for has been tested to see if they can be used in novel ways to overcome the problem of bacterial resistance.

Gordillo et al. (1993) conducted a study to determine the in vitro activity of azithromycin against enteric pathogens. It was found that *Camplyobacter* spp., *Escherichia coli*, *Shigella* spp., *Salmonella* spp. were sensitive to azithromycin.

Brogden and Campoli-Richards (1989) reviewed the antibacterial activity, pharmacokinetic properties and therapeutic potential of cefixime and found that the antibiotic was effective against many Enterobacteriaceae, *Haemophilus influenzae*, *Streptococcus pyogenes*, *Streptococcus pneumoniae* and *Branhamella catarrhalis* while showing little activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Arayne et al. (2002) reported that cefixime was active against both Gram-positive and Gram-negative strains of bacteria. *Escherichia coli* and *Staphylococcus aureus* were reported to be susceptible to cefixime.

According to a study conducted by Liu et al. (1997) testing the antibacterial activity of cefpodoxime in vitro, *Escherichia coli* and *Klebsiella pneumoniae* showed excellent activity. It had little effectiveness against *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*.

Knapp et al. (1988) tested the antibacterial activities of cefpodoxime, cefixime and ceftriaxone against various bacteria. It was reported that all three medicines inhibited the growth of *Branhamella catarrhalis*, *Neisseria meningitidis*, *Haemophilus influenzae*. Staphylococci, enterococci and *Pseudomonas aeruginosa* were shown to be resistant to the antibiotics taken.

Bantawa et al. (2019) reported that amoxicillin was ineffective against numerous bacteria like *Escherichia coli*, *Salmonella*, *Shigella and Vibrio* that were isolated from chicken, pork, buffalo and goat meat.

Norrby and Jonsson (1983) reported the effectiveness of norfloxacin against various strains of *Escherichia coli*, *Klebsiella* spp., *Proteus mirabilis*, indole-positive *Proteus* spp. *Serratia* spp., *Citrobacter* spp., *Enterobacter* spp. It was also found to be active against *Pseudomonas aeruginosa*, *Staphylococcus saprophyticus*, and enterococci which were resistant to nalidixic acid and cinoxacin.

In a review of the antibacterial activity of ofloxacin carried out by Monk and Campoli-Richards (1987), it was found that in vitro it showed more action against Gram-negative bacteria including *Citrobacter*, *Enterobacter, Klebsiella*, *Proteus*, *Salmonella* and *Shigella* species, *Yersinia enterocolitica*, *Escherichia coli*, *Neisseriaceae* and *Haemophilus influenzae*. It showed good activity against various streptococci and staphylococci.

There has been a rise in resistant strains of bacteria due to constant use of antibiotics. This has led to a need for innovation in antibiotic discovery and use. The discovery of new antibiotics is a time-consuming and often tedious process. Instead, a re-evaluation of antibiotics currently in use and testing them against bacteria for which they are not commonly prescribed can be a method for controlling the increase in resistant strains of bacteria.

METHODOLOGY

MATERIALS REQUIRED

Agar-agar, nutrient broth, distilled water, filter paper, petri plates, conical flasks, test tubes, forceps, cotton plug, sterile swab, autoclave, weighing machine, measuring cylinder, alcohol, newspaper, ruler, paper, pen etc.

ALLOPATHIC MEDICINES

Azithromycin, amoxycillin, cefixime, cefpodoxime, norfloxacin, ofloxacin

BACTERIAL STRAINS

Gram-negative bacteria (*Escherichia coli, Klebsiella, Vibrio parahaemolyticus*), Gram-positive bacteria (*Enterococcus, Staphylococcus aureus, Streptococcus iniae*)

NUTRIENT BROTH CULTURE

1.3 g of nutrient broth was weighed. It was added to 100 ml distilled water and mixed well. The broth was prepared in 100 ml conical flask and it was sterilised by autoclaving for 15 minutes and cooled to room temperature. The broth was then poured into sterilised test tubes (each test tube containing 5 ml broth) and closed using a cotton plug.

INOCULATING THE BROTH

The nutrient broth was inoculated. The cotton plug of the stock culture to be inoculated was loosened, and then the inoculating loop was flamed to red hot and cooled by waving for few seconds. The cotton plug from the stock culture tube was removed and the mouth was flamed. The cooled sterilised loop was inserted into the culture tube carefully without touching the sides to prevent contamination. A visible amount of the culture was scrapped and removed using the loop and mouth of the tube was plugged back carefully after flaming. By the same procedure, the cap was

introduced into the broth using the loop, tube mouth was flamed and recapped after the loop has been withdrawn. The inoculating loop was then sterilised again and the broth culture was gently rotated for the proper mixing of its content. The contents in each test tube were labelled with the names of the respective microbes and the date was noted. For sufficient bacterial growth, the inoculums were kept for 24 hours of incubation.

PREPARATION OF NUTRIENT AGAR (CULTURE MEDIA)

The medium was prepared using 1.3 g of nutrient broth and 2 g of agar. At first, both nutrient broth and agar were weighed out and made upto 100 ml using distilled water. It was poured into a conical flask and sterilised for 15 minutes in an autoclave. The medium was allowed to cool to an ear bearing heat (15^{o}C). Cooled nutrient agar was poured into petri dishes and it was left undisturbed till it set. It was then kept upside down. These petri dishes were used for the study.

PREPARATION OF FILTER PAPER DISC

Filter paper disc was prepared using a punching machine and sterilised using autoclave. The disc was then soaked in the medicines for a specific time and was used for anti-microbial sensitivity tests.

METHOD

The method used for antibacterial sensitivity was Kirby-Bauer disc diffusion method. A lawn culture of each bacterium was prepared using sterilised cotton swabs. A sterilised swab was dipped into the bacterial suspension, and moved side to side from top to bottom in the petri plate, leaving no space uncovered. The plate was rotated to 90^{o} and the same procedure was repeated so that the entire plate was coated with bacteria. This procedure was followed for all the different strains of bacteria.

Once the lawn had been prepared, the sterilised filter paper impregnated with the medicine to be tested was placed on the plate. This plate was incubated at 37^{o}C for 24-

48 hours. The names of the bacteria were labelled on each plate. The plate was examined for sensitivity (zone of inhibition). The radius of each zone was measured using a standard ruler in centimetres. If the compound is effective against bacteria at certain concentration, no colonies will grow where the concentration in the agar is greater than or equal to the effective concentration. This is the zone of inhibition which is a measure of the effectiveness of the compound. The larger the clear area around the filter paper, the more effective the compound.

KILLING OR DISPOSING

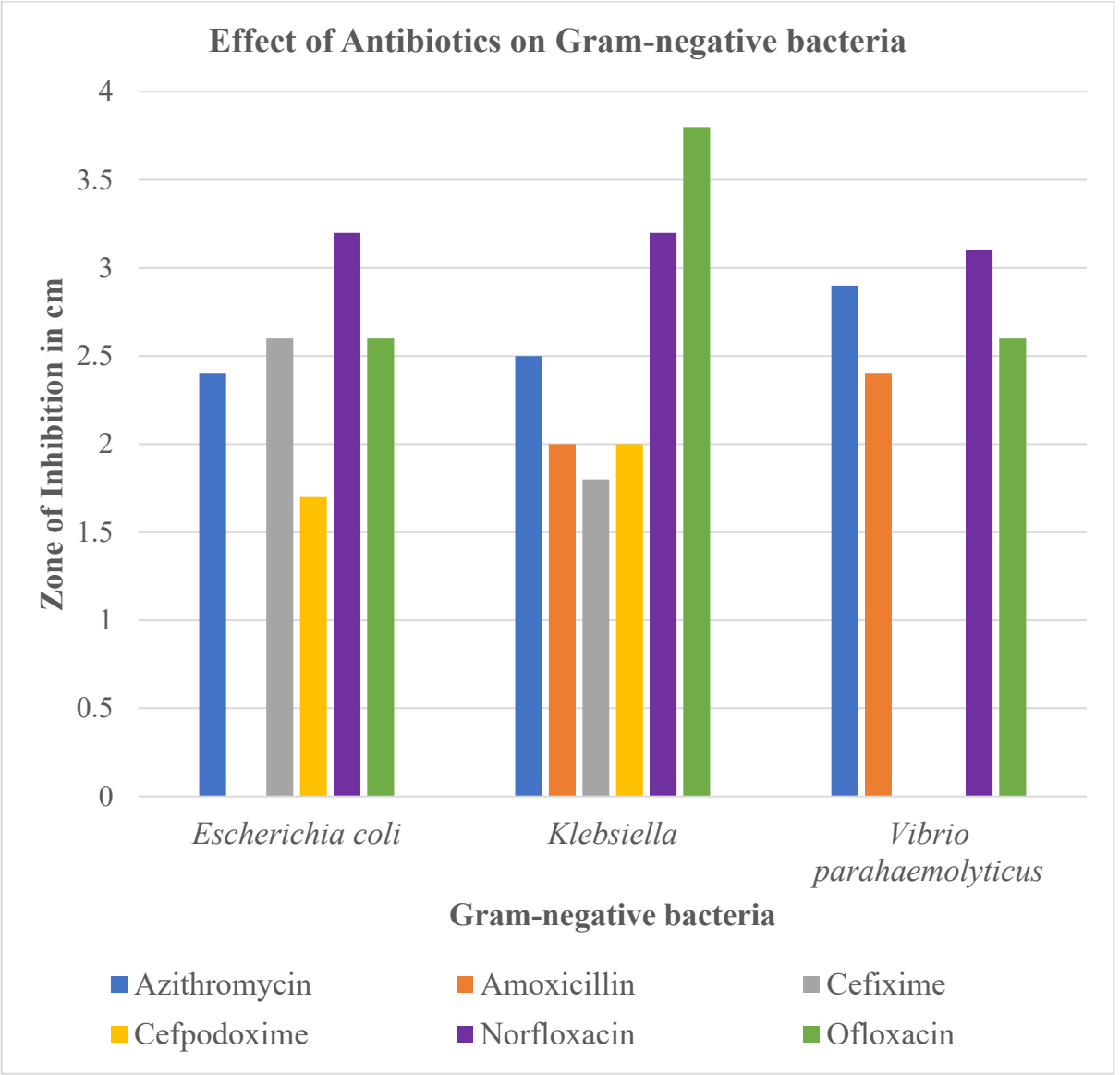
After the experiment, the bacteria were destroyed by autoclaving the plate for 20 minutes. All the glassware used for the experiment were also autoclaved to remove any contaminants.

OBSERVATIONS

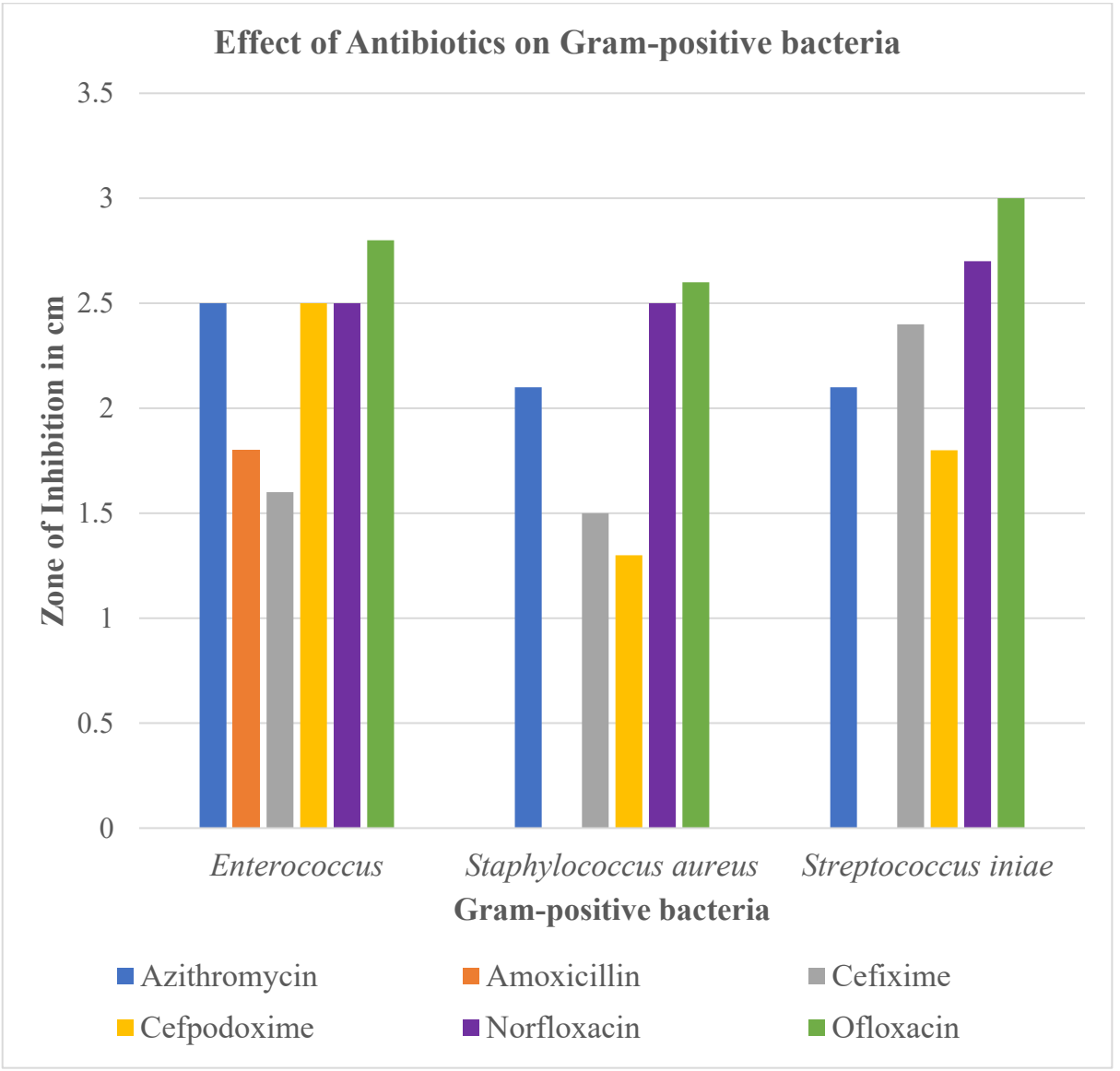
Medicines	Zone of Inhibition (Diameter in cm)					
	Gram-negative bacteria			Gram-positive bacteria		
	Escherichia coli	*Klebsiella*	*Vibrio parahaemolyticus*	*Enterococcus*	*Staphylococcus aureus*	*Streptococcus iniae*
Azithromycin	2.4	2.5	2.9	2.5	2.1	2.1
Amoxicillin	0	2	2.4	1.8	0	0
Cefixime	2.6	1.8	0	1.6	1.5	2.4
Cefpodoxime	1.7	2	0	2.5	1.3	1.8
Norfloxacin	3.2	3.2	3.1	2.5	2.5	2.7
Ofloxacin	2.6	3.8	2.6	2.8	2.6	3

Table showing Antibacterial activity of various antibiotics chosen against different bacteria

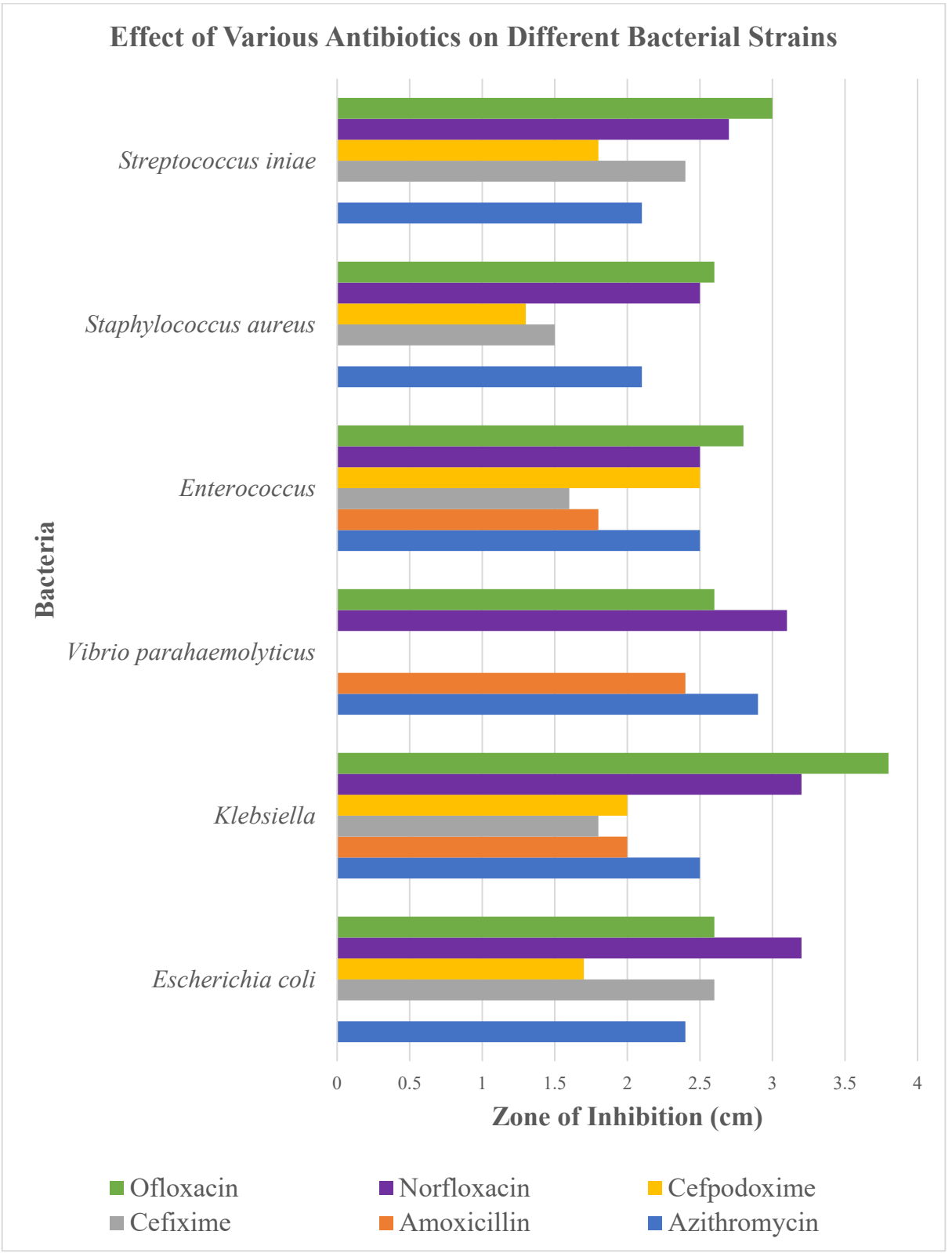
Photos showing the formation of Zone of Inhibition by various Antibiotics



Graph 1 showing Effect of Various Antibiotics on Different Gram-negative Bacteria



Graph 2 showing Effect of Various Antibiotics on Different Gram-positive Bacteria



Graph 3 showing Effect of Various Antibiotics on Different Bacterial Strains

RESULT

The antibacterial effect of commonly prescribed medicines (azithromycin, amoxicillin, cefixime, cefpodoxime, norfloxacin, ofloxacin) was studied against common infectious bacteria. The bacteria taken were 3 Gram-negative bacteria (*Escherichia coli, Klebsiella, Vibrio parahaemolyticus*) and 3 Gram-positive bacteria (*Enterococcus, Staphylococcus aureus, Streptococcus iniae*).

In the case of allopathic medicines, most medicines showed considerable effect against the bacteria taken in the study. Azithromycin, norfloxacin and ofloxacin showed effect against all the bacteria chosen. Cefpodoxime and cefixime were ineffective against *Vibrio parahaemolyticus* while amoxicillin was the least effective, showing no effect against *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus iniae*.

Escherichia coli was found to be the most sensitive to norfloxacin, with a zone of inhibition at 3.2 cm. The least effective medicine was amoxicillin which showed no inhibitory action against the bacteria. Amoxicillin is usually prescribed for respiratory infections and is ineffective against a bacteria like *E. coli* which is commonly found in the intestinal tract.

For *Klebsiella*, the medicine which showed the most inhibitory effect was ofloxacin which had a zone of inhibition of 3.8 cm. The least effective medicine was cefixime with a zone of inhibition of 1.8 cm.

Norfloxacin was found to have good inhibitory effect against *Vibrio parahaemolyticus* with a zone of inhibition of 3.1 cm. In contrast, it was completely resistant against cefixime and cefpodoxime.

Enterococcus was found to be sensitive to all the medicines taken in the study, with ofloxacin being the most effective with a zone of inhibition of 2.8 cm. Cefixime had the least effect on the bacteria with a zone of inhibition of 1.6 cm.

In the case of *Staphylococcus aureus* and *Streptococcus iniae*, ofloxacin showed the most inhibitory effect while amoxicillin was ineffective against both.

From the observations, it is evident that the most sensitive bacteria were *Klebsiella* and *Enterococcus*. The least sensitive bacterium was *Vibrio parahaemolyticus* which was resistant against cefixime and cefpodoxime. Ofloxacin was the most effective medicine against the bacteria selected in the study. It showed considerable inhibitory effect against all the bacteria. Amoxicillin was the least effective medicine showing no effect against *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus iniae*.

DISCUSSION

The present study aimed to analyse the antibacterial effect of commonly prescribed allopathic medicines (azithromycin, amoxicillin, cefixime, cefpodoxime, norfloxacin, ofloxacin) against 3 Gram-negative bacteria (*Escherichia coli, Klebsiella, Vibrio parahaemolyticus*) and 3 Gram-positive bacteria (*Enterococcus, Staphylococcus aureus, Streptococcus iniae*).

From the study, it was found that amoxicillin was the least effective medicine against the bacteria taken. Amoxicillin is a penicillin antibiotic usually recommended for treatment of respiratory infections like pneumonia, chest infections and ear infections. Yet in the present study it was found that the antibiotic showed greater effectiveness against the enteric bacteria (*Vibrio parahaemolyticus, Enterococcus, Klebsiella*) taken other than *Escherichia coli*.

According to Akhavan et al. (2022), amoxicillin is a beta-lactam antibiotic which shows bactericidal activity. It acts by binding to penicillin binding proteins which inhibits the formation of cross links in the bacterial cell wall. This leads to the lysis of the cell wall due to the activation of autolytic enzymes in the it.

Azithromycin is a broad-spectrum macrolide. It stops bacterial protein synthesis by binding to the 50S ribosomal subunit. This prevents the enzyme peptidyl transferase from adding amino acids to the growing peptide chain (Patel & Hashmi, 2022). Azithromycin is usually prescribed for respiratory infections, chest infections and dental abscesses. However in the present study it was seen to be more effective against the enteric bacteria taken. *Vibrio parahaemolyticus* is a bacteria causing gastroenteritis that is commonly found in the intestinal tract. It was very sensitive to azithromycin showing a zone of inhibition of 2.9 cm. In the current study, the antibiotic was found to exhibit greater activity against the Gram-negative (*Escherichia coli, Klebsiella,*

Vibrio parahaemolyticus) bacteria taken when compared to the Gram-positive bacteria (*Enterococcus, Staphylococcus aureus, Streptococcus iniae*).

Cefixime and cefpodoxime are both cephalosporins. The mechanism of action of cephalosporins is similar to that of penicillin. They prevent the synthesis of bacterial cell wall by binding to the penicillin-binding protein and inhibiting its activity (Bui & Preuss, 2022).

Cefixime is a broad-spectrum cephalosporin. It showed inhibitory activity towards all the bacteria taken except *Vibrio parahaemolyticus*. This result is in contrast to the study carried out by Brogden et al. (1989), where *Staphylococcus aureus* and *Enterococcus* were found to be resistant to cefixime. In a more recent study conducted by Arayne et al. (2002), it was found that cefixime did have an effect on *Staphylococcus aureus*.

Cefpodoxime is a cephalosporin which is used to treat respiratory infections such as bronchitis and pneumonia. It showed no effect against *Vibrio parahaemolyticus* though other enteric bacteria were seen to be susceptible to it. *Enterococcus* was highly susceptible to cefpodoxime showing a zone of inhibition of 2.5 cm which is in contrast to the previous studies (Todd, 1994; Liu et al., 1997).

Norfloxacin and ofloxacin are fluoroquinolones. They act by preventing the action of type II DNA topoisomerases so that bacterial transcription and DNA replication are interrupted (Bethesda, 2020). They showed the most activity against the bacteria chosen. All the bacteria taken were susceptible to both antibiotics.

Ofloxacin was more effective than norfloxacin as evident by the greater zone of inhibitions created by the former. According to Monk et al. (1987), ofloxacin shows more effectiveness against Gram-negative in comparison to Gram-positive though such a distinction cannot be seen in the present study.

On the other hand, Gram-negative bacteria were more sensitive to norfloxacin than Gram-positive. All the Gram-negative bacteria taken showed zones of inhibition greater than 3 cm. This is accordance with the studies carried out by Goldstein (1987).

In the present study, it was found that medicines prescribed for respiratory ailments (amoxicillin, azithromycin) showed greater activity against enteric bacteria. These medicines show potential to be also used in the treatment of gastrointestinal diseases. The reduced effect of these medicines against the bacteria found in the respiratory tract could be due to the development of resistant strains.

CONCLUSION

The antibacterial activity of commonly prescribed allopathic medicines (azithromycin, amoxicillin, cefixime, cefpodoxime, norfloxacin and ofloxacin) was tested against 3 Gram-negative (*Escherichia coli, Klebsiella, Vibrio parahaemolyticus*) and 3 Gram-positive (*Enterococcus, Staphylococcus aureus, Streptococcus iniae*) bacteria using the Kirby-Bauer disc diffusion method.

Most of the bacteria were sensitive to the medicines taken. The most sensitive bacteria were *Klebsiella* and *Enterococcus*. *Klebsiella* showed zones of inhibition ranging from 1.8 – 3.8 cm while for *Enterococcus* the range was from 1.6 – 2.8 cm. Ofloxacin was the most effective medicine showing good inhibitory effect against all the bacteria taken in the study. On the other hand, amoxicillin was the least effective medicine having no effect on three of the six bacteria taken. From the study it was observed that medicines prescribed for respiratory ailments (azithromycin, amoxicillin) showed substantial inhibitory activity against enteric bacteria (*Vibrio parahaemolyticus*, *Enterococcus*, *Klebsiella*). This shows that these antibiotics also have the potential to treat intestinal ailments.

BIBLIOGRAPHY

Akhavan, B. J., Khanna, N. R., & Vijhani, P. (2022). *Amoxicillin*. StatPearls Publishing.

Arayne, M. S., Sultana, N., Khanum, F., & Ali, M. A. (2002). Antibacterial studies of cefixime copper, zinc and cadmium complexes. *Pakistan journal of pharmaceutical sciences*, *15*(1): 1–8.

Aslangul, E., Ruimy, R., Chau, F., Garry, L., Andremont, A., & Fantin, B. (2005). Relationship between the level of acquired resistance to gentamicin and synergism with amoxicillin in Enterococcus faecalis. *Antimicrobial Agents and Chemotherapy*, *49*(10): 4144–4148.

Bantawa, K., Sah, S. N., & Subba, L. D. (2019). Antibiotic resistance patterns of Staphylococcus aureus, Escherichia coli, Salmonella, Shigella and Vibrio isolated from chicken, pork, buffalo and goat meat in eastern Nepal. *Biomedical Centre Research Notes*, *12*: 766.

Baron, S. (Ed.). (1996) *Medical Microbiology*. University of Texas Medical Branch.

Brogden, R. N., & Campoli-Richards, D.M. (1989). Cefixime. *Drugs*, *38*: 524–550.

Bui, T., & Preuss, C. V. (2022). *Cephalosporins*. StatPearls Publishing.

Fisher, M. C. (2006). *Immunizations and Infectious Diseases*. American Academy of Pediatrics.

Goldstein, E. J. (1987). Norfloxacin, a fluoroquinolone antibacterial agent: Classification, mechanism of action, and in vitro activity. *The American journal of medicine*, *82*(6B): 3–17.

Gomes, C., Martínez-Puchol, S., Palma, N., Horna, G., Ruiz-Roldán, L., Pons, M. J., & Ruiz, J. (2017). Macrolide resistance mechanisms in Enterobacteriaceae: Focus on azithromycin. *Critical reviews in microbiology*, *43*(1): 1–30.

Gordillo, M. E., Singh, K. V., & Murray, B. E. (1993). In vitro activity of azithromycin against bacterial enteric pathogens. *Antimicrobial Agents and Chemotherapy*, *37*(5): 1203–1205.

Hutchings, M. I., Truman, A. W., & Wilkinson, B. (2019). Antibiotics: past, present and future. *Current Opinion in Microbiology*, *51*: 72–80.

Knapp, C. C., Sierra-Madero, J., & Washington, J. A. (1988). Antibacterial activities of cefpodoxime, cefixime and ceftriaxone. *Antimicrobial Agents and Chemotherapy*, *32*(12): 1896–1898.

Liu, Y. C., Huang, W. K., & Cheng, D. L. (1997). Antibacterial activity of cefpodoxime in vitro. *Chemotherapy*, *43*(1): 21–26.

Monk, J. P., & Campoli-Richards, D. M. (1987). Ofloxacin. *Drugs*, *33*: 346–391.

Murray, C. J., Ikuta, K. S., & Sharara, F. (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *The Lancet*, *399*(10325): 629–655.

Norrby, S. R., Jonsson, M. (1983). Antibacterial activity of norfloxacin. *Antimicrobial Agents and Chemotherapy*, *23*(1): 15–18.

Patel, P. H., & Hashmi, M. F. (2022). *Macrolides*. StatPearls Publishing.

Todd, W. M. (1994). Cefpodoxime proxetil: a comprehensive review. *International Journal of Antimicrobial Agents*, *4*(1): 37–62.

Ventola, C. L. (2015). The antibiotic resistance crisis. *Pharmacy and Therapeutics*, *40*(4): 277–283.

Werth, B. J. (2022). *Overview of Antibiotics*. Merck & Co.