International Journal of Research in Agriculture, Biology & Environment (IJAGRI)

E-ISSN : 2582-6107

DOI: 10.47504/IJAGRI.2022.3.4.1

Volume 3 (4) 2022
Oct - December -2022

Veterinary Drug Prescribing Practices at Ateso Veterinary Clinic of Masha Woreda, Sheka Zone, South West Ethiopia

Esayas Balcha, Teshager Shawano

[1]Animal Health Institute, Wolaita Sodo Branch, Ethiopia

[2]School of Veterinary Medicine, Wolaita Sodo University, Ethiopia

ABSTRACT

The rational use of drugs in veterinary medicine has various significances, such as reducing the risk of drug resistance, increasing efficacy, reducing drug residue, and decreasing adverse drug reactions. The objective of this study is to evaluate types of rational use of veterinary drugs prescribed by veterinarians in the veterinary clinics of the Masha district. A sample was selected using a systematic random sampling method and the sampling unit was an animal patient encountered at Ateso veterinary clinic for the treatment of acute and/or chronic illness. A retrospective study was conducted to assess veterinary drug prescribing practices at Ateso woreda veterinary clinics in the south west areas of Ethiopia. A total of 920 cases were recorded from the case registration books at the Ateso Veterinary clinic for diseases treated between January 2021 and February 2022. The study indicates that in Ateso veterinary clinic, 111(12.1%) young, 548(59.6%) adult and 261(28.4%) were old. In this retrospective study, 654(71.1%) cattle, 62(6.7%) chicken, 66(7.2%) goat and 138(15.0%) were sheep in diagnosed animals. Regarding the agro-ecological partition in study area, 542(58.9%), 129(14.0%) and 249(27.1%) of diagnosed animals were highland, lowland and midland respectively. The study results showed that for a total of 920 cases diagnosed at clinic, 1788 different drugs were prescribed, with an average per encounter of 1.9. Among the total drugs, Penstrep (31.7%), Albendazole (23.3%), Oxytetracycline (19.4%), Ivermectine (12.3%, Sulfa drugs (6.7%), Isomitamidium chloride (3.7%) and Veridium(2.9%) were the most leading prescribed drugs. All drugs were prescribed by the generic name without any laboratory support of the disease. The prescribing practices showed 51.1 % of antibiotics and 23.3 % of anthelmintic was prescribed for veterinary diseases treatment at Ateso veterinary clinic. Of the prescribed drugs, 7 % Anthelmentics (Albendazole) was prescribed irrationally to treat diseases that were tentatively diagnosed as infectious diseases. Similarly, 2.1 % Antibiotics were prescribed for parasitic disease. In conclusion, this study revealed problems in antibiotics and Anthelmintics use, description of routes of administration and length of treatment, and shortage of laboratory diagnostic facilities. Therefore, veterinary drugs particularly Antibiotics and Anthelmintics should be used appropriately to safeguard the public from residual drug impacts and resistance development.

Key words: South-West Ethiopia, Veterinary Clinic, Veterinary Drug, Woreda.

1. NTRODUCTION

Antimicrobials are used in the clinical practice of human and veterinary medicine throughout the world. The use of veterinary drugs is one of the major strategies for alleviating the incessant disease constraint in livestock production systems. Veterinary drugs are used in the livestock sector either rationally or irrationally as therapeutic, prophylactic, and growth promotion. (Vitomir *et al*., 2011, WHO, 2012).

The rational approach to therapeutics requires careful evaluation of the health problem in each species of animals and selecting appropriate therapeutic strategies. Besides rational use of drugs, is based on the use of the right drug, at the right dosage, right cost, and right time which is well reflected in the World Health Organization (Matter *et al*., 2007, Rehan *et al*., 2001, WHO, 2012).

Irrational use of drugs is defined as “too many medicines are prescribed per patient, injections are used where oral formulations would be more appropriate, antimicrobials are prescribed in inadequate doses or duration, antibiotics prescribed for non-bacterial infections, prescriptions do not follow clinical guidelines, and self-medicate inappropriately or do not adhere to prescribed treatment (WHO, 2012). Irrational use of drugs in veterinary medicine and the need for control of their use becomes an even bigger problem when used on food-producing animals. Here, there is the possibility that minimal quantities of drugs and their metabolites (residues) which remain in edible tissues or in animal products (meat, milk, eggs, honey) induce certain harmful effects in humans as potential consumers of such food (Sanders, 2007)

Antimicrobial therapy failures may occur when the pathogenic microorganism is unknown and a combination of two or more drugs is administered empirically. To avoid these mistakes, clinically confirmed, effective antimicrobial combinations should be used (Vitomir *et al*., 2011). Improper use of drugs may cause ineffective treatment, unnecessary wastage of resources and may harm the patient (DACA, 2006). To prevent this risk, it is necessary to use drugs rationally that is to use them only when they are indicated, in the right way, at the right time, in the right dose, and respect the withdrawal period. Additionally, it should regularly control sensitivity to antimicrobial agents and regulate the residue of antimicrobial agents commonly used in veterinary practice (Barbosa *et al*., 2005, Vitomir *et al*., 2011). Selection of treatment requires cost/benefit analysis, particularly in food animals. Its efficacy, safety with minimal adverse effects, and minimal residues in food animals should be also given due attention. Drug choice depends on the individual patient and prescription; whenever written it should indicate the species of animal, the age, sometimes breed, the dose of the drug in the formulations available locally, and the duration of treatment (DACA 2006, Rehan *et al*., 2001). Advice on nutritional support and nursing care is also very important to ensure rational therapeutics (Rehan *et al*., 2001).

Overuse of antimicrobials (VMD (2008) and anthelmintic (Geary *et al*., 2010) in veterinary medicine for food-producing and companion animals, favors the development of antimicrobial and anthelmintic resistance. This drug resistance is a growing problem and some of the common causes that contribute to the development of antimicrobial resistance are unnecessary to use of antimicrobial drugs, inappropriate doses, inadequate duration of therapy, and use of irrational antimicrobial fixed-dose drug combinations (Soulsby, 2005).

Currently, in the clinical practice of human and veterinary medicine throughout the world, large amounts of antibiotics are used. Equally, many scientists intensively work on the discovery and synthesizing of new drugs with a broader antimicrobial spectrum, stronger action, and a more satisfactory safety profile. They are now widely accepted as a global standard for problem identification and are used in developing countries (WHO, 1993, Laing, 2001)

2. STATEMENT OF THE PROBLEM

In Ethiopia, a survey conducted on human subjects at hospitals revealed irrational drug use (WHO, 2003, Endale, 2013). However, in veterinary practice, a few published reports on the rational use of veterinary drugs in the country in general, although different studies were conducted irrational use of drugs in veterinary clinics (Beyene, 2015). However, in the Keffa zone Masha district, the rational use of veterinary drugs was not studied and published. Therefore, the Objective of this study is:

- To evaluate types of rational use of veterinary drugs prescribed by veterinarians in the veterinary clinics of the Masha district.

3. LITERATURE REVIEW

The term antibiotic was coined from the word „antibiosis" which means „against life". An antibiotic or an antibacterial compound is a drug issued to treat and prevent bacterial infections. They may either inhibit the growth or kill the bacteria. In the past, antibiotics were considered to be organic compounds produced by one microorganism which are toxic to other microorganisms (Russell, 2004). Antibiotics are widely used in healthy food-producing animals to promote growth and prevent diseases. This practice favors the emergence and spread of resistant bacteria in both animal and human populations. The routine use of antimicrobials in vast numbers of healthy animals is likely to result in the emergence and spread of antimicrobial-resistant bacteria and cause resistant infections in animals and humans (Gasbarre, 2009).

Anthelmintic resistance is becoming an increasing global problem resulting from the misuse of these drugs. Resistance to anthelmintic by ruminant nematode parasites is a growing problem throughout the world (Gasbarre, 2009). Food animals and foods of animal origin are traded worldwide; thus, drug resistance affecting the food supply of one country becomes a potential problem for other countries (Amane and Kop, 2011).

DOI: 10.47504/IJAGRI.2022.3.4.1

A. *Classification of Antibiotics*

There are several ways of classifying antibiotics but the most common classification schemes are based on their molecular structures, mode of action, and spectrum of activity (Calderon and Sabundayo, 2007). Some common classes of antibiotics based on chemical or molecular structures include Beta-lactams, Macrolides, Tetracyclines, Quinolones, Aminoglycosides, Sulphonamides, Glycopeptides, and Oxazolidinones (van Hoek *et al.*, 2011; Frank and Tacconelli, 2012; Adzitey, 2015).

B. The β-lactams

Members of this class of antibiotics interfere with proteins essential for the synthesis of the bacterial cell wall, and in the process either kill or inhibit their growth. More succinctly, certain bacterial enzymes termed Penicillin-Binding Protein (PBP) are responsible for cross-linking peptide units during the synthesis of peptidoglycan. Members of beta-lactam antibiotics can bind themselves to these PBP enzymes, and in the process, they interfere with the synthesis of peptidoglycan resulting in lysis and cell death (Heesemann, 1993). The β-lactams constitute a group of antibiotics including penicillins, cephalosporins, monobactams, and carbapenems which inactivate glycopeptide transpeptidases, thereby inhibiting bacterial cell wall synthesis. This leads to its main bactericidal properties via cell lysis (Xia et al., 2016, Bush *et al*., 2016).

C. Penicillins

The first antibiotic, penicillin, which was first discovered and reported in 1929 by Alexander Fleming, was later found to be among several other antibiotic compounds called penicillins. (McGeer *et al*., 2001). Penicillins are involved in a class of a diverse group of compounds, most of which end in the suffix -cillin. They are beta-lactam compounds containing a nucleus of 6-animopenicillanic acid (lactam plus thiazolidine) ring and other ringside chains (Zahner and Maas, 1972). Members of the Penicillin class include Penicillin G, Penicillin V, Oxacillin (dicloxacillin), Methicillin, Nafcillin, Ampicillin, Amoxicillin, Carbenicillin, Piperacillin, Mezlocillin, and Ticarcillin (Boundless, 2016).

D. Cephalosporin

Members of this group of antibiotics are similar to penicillin in their structure and mode of action. They form part of the most commonly prescribed and administered antibiotics; more succinctly, they account for one-third of all antibiotics prescribed and administered by the National Health Scheme in the United Kingdom (Talaro and Chess, 2008). The first known member of this group of antibiotics was first isolated by Guiseppe Brotzu in 1945 from the fungus Cephalosporium acremonium. Although the drug was first isolated by Guiseppe Brotzu, it was Edward Abraham who got the credit to patent it has been able to extract the compound. Cephalosporins are used in the treatment of bacterial infections and diseases arising from Penicillinase-producing, Methicillin-susceptible Staphylococci and Streptococci, Proteus mirabilis, some Escherichia coli, Klebsiella pneumonia, Haemophilus influenza, Enterobacter aerogenes and some Neisseria (Pegler and Healy, 2007).

Cephalosporins are increasingly more effective against Gram-negative pathogens. Cephalosporins have a variety of side chains that enable them to get attached to different penicillin-binding proteins (PBPs), to circumvent the blood-brain barrier, resist breakdown by penicillinase-producing bacterial strains, and ionize to facilitate entry into Gram-negative bacterial cells (Abraham, 1987).

E. Tetracyclines

Tetracycline was discovered in 1945 from a soil bacterium of the genus Streptomyces by Benjamin Duggar (Sanchez et al., 2004). The first member of this class was chlortetracycline (Aureomycin). Members of this class of antibiotics are grouped into different generations based on the method of synthesis. Those obtained by biosynthesis are said to be the first generation. Members include Tetracycline, Chlortetecycline, Oxytetracycline, and Demeclocycline. Members such as Doxycycline, Lymecycline, Meclocycline, Methacycline, Minocycline and Rolitetracycline are considered the Second generation because they are derivatives of semi-synthesis. Those obtained from total synthesis such as Tigecycline are considered to be third generation (Fuoco, 2012). Their target of antimicrobial activity in bacteria is the ribosome. They disrupt the addition of amino acids to polypeptide chains during protein synthesis in this bacterial organelle (Medical News Today, 2015).

DOI: 10.47504/IJAGRI.2022.3.4.1

F. Aminoglycosides

The first drug to be discovered among members of this class of antibiotics was streptomycin, first isolated in 1943 (Mahajan and Balachandran, 2012). Streptomycin has been greatly used against Mycobacterium tuberculosis, the causal agent of tuberculosis among humans. They are obtained from soil Actinomycetes. Aminoglycosides have a broad spectrum of antibacterial activity. They can inhibit the protein synthesis in bacteria by binding to one of the ribosomal subunits (Peterson, 2008). Also effective against aerobic Gram-negative rods and certain Gram-positive bacteria. The oldest known aminoglycoside, as earlier inferred is Streptomycin which has been used severally in treating bubonic plague, tularemia, and tuberculosis (Talaro and Chess, 2008).

Notwithstanding its effectiveness against a wide array of infections, streptomycin was found to be highly toxic. This unfortunate feature of the drug necessitated the need to search for new members of aminoglycosides that would still be effective against bacteria but less toxic to humans. The search was fruitful with the discoveries of antibiotics such as Gentamicin, Neomycin, Tobramycin, and Amikacin (Gilbert, 2000)

G. Sulphonamides

Sulphonamides are reported, the first group of antibiotics used in therapeutic medicine, and they still play a very important role in medicine and veterinary practice (Eyssen *et al*., 1971). Sulphonamides inhibit both Gram-positive and Gram-negative bacteria such as Nocardia, E. coli, Klebsiella, Salmonella, Shigella and Enterobacter, Chlamydia trachomatis and some Protozoa, and are widely used in the treatment of various infections including tonsillitis, septicemia, meningococcal meningitis, bacillary dysentery and some urinary tract infections (Eyssen *et al*., 1971). Studies have shown that Sulphonamides are also able to impede cancerous cell agents (Stawinski *et al*., 2013; Xu *et al*., 2014). The original antibacterial sulphonamide (also spelled sulfonamide by some Workers) is synthetic antimicrobial agents that contain the sulphonamide group (Henry, 1943). Although sulphonamides are adjudged good and effective in treating various diseases and infections, they are recommended and administered with caution because of their toxicity and side effects, some of which include urinary tract disorders, hemolytic anemia, porphyria, and hypersensitivity reactions (Slatore and Tilles, 2004; Choquet-Kastylevsky *et al*., 2002).

H. Classification of Anthelmintic

Anthelmintic is the most popular way to treat nematode infections (Crawford *et al*., 2006). Broad-spectrum anthelmintic has helped to reduce the incidence of nematode infections. Generally, anthelmintic groups are effective against both the immature and mature stages of virtually all of the important gastrointestinal nematodes, as well as many other intestinal parasites (Köhler, 2001). In addition to synthetic drugs, there are three groups of synthetic anthelmintic.

I. Benzimidazoles

Benzimidazoles are a class of products used mainly to treat nematode infections in humans and animals (Stepek *et al.*, 2004). Benzimidazole structures are diverse, based on chemical substitutions at different positions of the Benzimidazole nucleus (Nagawade and Shinde, 2006). Chemically, benzimidazoles are heterocyclic aromatic organic compounds. This bicyclic compound consists of the fusion of *benzene* and *imidazole*. The most prominent Benzimidazole compound in nature is *N-ribosyl-dimethyl* benzimidazoles, which serve as an axial ligand for cobalt in vitamin B12. The Benzimidazoles group includes many members such *as* Mebendazole, Flubendazole, Fenbendazole, Oxfendazole, Oxibendazole, Albendazole, Albendazole sulfoxide,Thiabendazole, Thiophanate, Febantel, Netobimin, and Triclabendazole. They are relatively safe for ruminants, although Albendazole has been shown to have teratogenicity effects, and should not be used in early gestation (Zajac, 2006). These Benzimidazoles affect the microtubules of the worm by binding to B-tubulin, which inhibits the polymerization of tubulin and the formation of microtubules (Köhler, 2001). The lack of microtubules inhibits many cellular functions such as transport, cell division, neural transmission, and cell differentiation, ultimately leading to cell death in the worm (Prichard, 2005).

Benzimidazoles have greater activity in the gut of small ruminants than in large ruminants. Benzimidazole metabolism in large ruminants is more extensive than in small ruminants. In ruminants, benzimidazoles go to the rumen directly, then slowly into the remainder of the gastrointestinal tract; so, there is no need to repeat the dose for greater efficacy except for goats. In goats, is essential to repeat the doses for greater efficiency. The absorption of Fenbendazole is slow in ruminants but is more rapid in monogastric. Mostly the fecal route eliminates Fenbendazole. The liver is the main target tissue in all species tested. The metabolism of Fenbendazole, Febantel, and Oxfendazole is similar in most species that have been investigated (European medicines agency, 2004).

DOI: 10.47504/IJAGRI.2022.3.4.1

J. Imidazothiazoles and tetra hydro pyrimidine

Imidazothiazoles are nicotinic drugs. They affect the nervous system of worms; consequently, they cause sustained muscle contraction, leading to paralysis in nematodes and other parasites. Levamisole, Tetrahydropyrimidine (e.g. Pyrantel and Morantael), and some other structurally related compounds are the main nicotinic drugs (Köhler, 2001). Imidazothiazoles are rapidly absorbed from the digestive tract, metabolized in the liver, and eliminated in the urine largely as metabolites in two days. They are found in many formulations (suspension, paste, drench, or tablets), and used as broad-spectrum anthelminthic. Imidazothiazoles in ruminants are highly effective against the common adult gastrointestinal nematodes and lungworms, and many larval stages. However, pyrantel activity is limited to adult gastrointestinal nematodes (Merck Veterinary Manual, 2008).

K. Macrocyclic lactones

Macrocyclic lactones are a class of anthelmintic used mainly to control nematode and arthropod parasites. The macrocyclic lactones family includes avermectin, doramectin, abamectin, milbemycin, and moxidectin. However, avermectin is widely used as an anthelmintic in veterinary medicine and to treat onchocerciasis or river blindness in humans (Cully *et al*., 1994). Avermectin and milbemycin compounds are closely related members of macrocyclic lactones. Both are chemicals produced through fermentation by soil actinomycetes from the genus *Streptomyces* and have similar spectra of activity (Hennessy and Alvinerie, 2002).

The avermectins/milbemycin bind to glutamate and gamma-aminobutyric acid (GABA)- gated causing a hyper-polarization of nerve or muscle cells, leading to paralysis of movement, paralysis of the pharyngeal pump, and inhibition of ovipositional due to effect on uterus muscles. Therefore, nematodes are unable to move, feed, or reproduce. Finally, they are quickly removed from the host animal (Prichard, 2001). A recent study in cattle demonstrated that orally administered avermectin/milbemycin drugs were significantly more effective than when administered by injection or pour-on (Leathwick and Miller, 2013).

L. Antiprotozoal Drugs

Animal diseases are perhaps the most important limitation to animal production in developing countries. The prototype protozoa of the animal world area trypanosomes, babesia, theileria, and anaplasma. These are transmitted through a vector to the final host and cause great economic losses (Akhter *et al.*, 2010). Blood protozoa are introduced into new areas and countries due to the free movement of livestock from one place to another. All domestic animals are prone to infection but buffalo, cattle, and pigs serve as reservoir hosts (Soulsby, 1982).

Control of parasitic diseases is achieved by different means, such as biological control, genetic control, and by chemotherapy and vaccines. The most effective and confirmed method of control is through the strategic use of drugs that kill the parasites without harming the host. Many of the standard chemotherapies are used today (Cheesman, 2000).

The treatment of Babesiosis is dependent upon the availability of a particular drug on the market. Quinuronium sulfate, Pentamidium, Amicarbalide, Diminazene aceturate, and imidocarb are the most commonly used drugs (Urquhart et al, 1988). Remedy for Theileriosis is best observed by Buparvaquone, which is a more effective and reliable drug than any other in field condition (Nasir, 2000). Tetracyclines (Chlortetracycline, Tetracycline, and Oxytetracycline) are used for the treatment of anaplasmosis (Urquhart *et al*, 1988).

M. Acaricides

Acaricides are pesticides that kill members of the arachnid subclass *Acari*, which includes ticks and mites. Acaricides are used both in medicine and agriculture, although the desired selective toxicity differs between the two fields. Ticks are economically the most important pests of cattle and other domestic species in tropical and subtropical countries (Jongejan and Uilenberg, 1994). More than 80% of the world cattle population is infested with ticks (FAO, 1984), which cause harm to animals through blood loss, general stress and irritation, depression of immune function, damages to hides and skins (Ghosh *et al.*, 2007). Although, economic losses due to ticks are mainly due to the diseases which they transmit (Garcia, 2003), financial losses associated with nagging irritation and depreciation of the value of skins and hides (up to 20–30%) are also significant (Biswas, 2003).

Susceptibility and Resistance of animals to tick infestation have been influenced by several factors including; species, age, sex, season, breed, photoperiod and management. Chemical application of acaricide is still the most widely used way of control,

DOI: 10.47504/IJAGRI.2022.3.4.1

although there are reports of tick resisting to many active principles in different countries (Martins et al., 1995) that are applied by dipping, spraying or pour-on which is considered as one of the best methods.

The current tick control strategies aim to reduce ticks numbers to acceptable levels, to prevent production loss, minimize chemical residue risks, and reduce the reliance on chemicals by utilizing control with alternative treatments for different herd group's (Ghosh et al., 2007).

4. MATERIALS METHODS

N. Study Areas

The study was conducted in the Sheka Zone, at Masha Woreda in Ateso veterinary clinic which is located in the Southwestern Ethiopian people's regional state. Geographically, Sheka zone, Masha town is found 675km southwest of Addis Ababa. Woreda is located between 7^0 24` to $7^0$ 52`N latitude and 35^0 13` to $35^0$ 35`E longitudes and has an altitude ranging from 500-2800 meters above sea level (m.a.s.l). It has an area of 90192 hectares and about 209,000 human populations of which 89.8% live in the rural part of the region. The main occupation of the rural population is mixing farming practices whereby crops and livestock are managed. The livestock population of the Woreda is 170,000 cattle, 192,450 sheep, 38,980 goats, 286,246 chickens, 13,796 horses, 60 pigs, 2103 mules and 67 donkeys (BFEDDSP, 2014).

Agro-ecologically, the Woreda is divided into lowland (3%), midland (17%), and highland (80%). The average annual rainfall ranges between 400 mile meter & 2000mile meter (mm) and the mean temperature ranges between 15^0C to 27^0C respectively. The rainfall is with a short rainy season from March to May and a long rainy season from June to November followed by a dry season from January to February (BFEDDSP, 2014).

O. Study Design.

A retrospective and cross-sectional study was to evaluate the types of rational use of veterinary drugs prescribed by veterinarians in the veterinary clinics of the Masha district. A sample was selected using a systematic random sampling method, and the sampling unit was an animal patient encountered at both veterinary clinics for the treatment of acute and/or chronic illness. Secondary data are the source of information. Accordingly, data were collected from the case book records from the office of both clinics by using systematic random sampling.

P. Study Population

The study was conducted between January 2021 and February 2022 on food animal patient cattle, sheep, goats, and chickens of all ages and sex groups) that were admitted to the Ateso veterinary clinic and treated with drugs. All other non-food animals (e.g., pets and equines) were excluded from the study because of the study area that is in Masha District of Ateso veterinary clinic animals which come to clinic are almost food animals rather than pets and equines.

Q. Data Collection

Data were collected in data collection format retrospectively using case registration books at the clinics, specific types of data necessary to measure the prescribing indicators were recorded for each animal patient encounter and entered directly into an ordinary prescribing indicator form. In this current study, prescriptions that contain the animal's characteristics (age, sex, breed, body condition, clinical signs, and symptoms observed); disease diagnosis (name, empiric or physical clinical examination) prescribed drugs (type, naming (generic or brand), number of drugs prescribed, route of administration, duration of treatment); Accordingly, the evaluation of the rational use of veterinary drugs were made based on generic prescription and antimicrobials and anthelmintic prescribed for tentatively diagnosed clinical cases.

R. Data Analysis

All data in the ordinary prescribed indicator recording form were entered into a Microsoft Excel spreadsheet (version 2010) and imported and analyzed using SPSS (Version 20). Descriptive statistics such as frequencies, percentages, and cross-tabulation were used to describe the characteristics of the drugs. A Chi-square test was used to compare categorical variables will appropriate.

DOI: 10.47504/IJAGRI.2022.3.4.1

S. Prescribing Indicators

No available guidelines for prescribing indicators used in veterinary medicine indicators were pretested and slightly modified to match with clinical practice in veterinary medicine so that they could be used easily to provide accurate data. The final versions of the pretested indicators are as follows:

- ✓ An average number of drugs prescribed per encounter were calculated by dividing the total number of different drug products prescribed by the number of encounters surveyed to measure the degree of polypharmacy.
- ✓ Percentages of drugs prescribed by the generic name were calculated by dividing the number of drugs prescribed by the generic name by the total number of drugs prescribed, multiplied by 100 to measure the tendency of prescribing by generic name.
- ✓ Percentage of encounters in which antimicrobials, anthelmintic, and other drugs prescribed were was calculated by dividing the number of patient encounters in which the drug was prescribed by the total number of drugs prescribed and multiplied by 100 to measure the overall use of commonly overused (irrationally prescribed) and costly forms of drug therapy.
- ✓ Percentage of drugs prescribed for each disease encountered was calculated by dividing the number of drugs prescribed for each disease by the total number of encounters and multiplied by 100. Commonly drugs used in vet clinics are:
    - ❖ Oxytetracycline
    - ❖ Ivermectin
    - ❖ Pen strep
    - ❖ Sulfa drug
    - ❖ Albendazole
    - ❖ Veridium
    - ❖ Isomitamidium chloride

5. RESULT

A total of 920 presented cases to clinics were assessed from Ateso district veterinary clinics. A retrospective study has shown that 1788 drugs were prescribed, and the average number of drugs per encounter was 1.9 with a maximum of 3 and a minimum of 1. Among 1788 prescribed drugs, 308(31.7%) Penstrep, 226(23.3%) Albendazole and 189(19.4%) Oxytetracyclines were most commonly used in Ateso veterinary clinic (Table2). Among the total 920 patient encounters, the relationship between tentatively diagnosed diseases and drugs prescribed was evaluated. The results showed that Oxytetracycline was prescribed for 16(8.5%) treatment of Black leg, 2 (1.1%) Bloat, 5(2.6%) Bovine mastitis, 10(5.3%) Lumpy and Skin Disease, 8(4.2%) Newcastle disease, 116(61.4%) Pasteurolosis, 8(4.2%) Pneumonia and 17(%8.9) Salmonellae. The study Show that in Ateso veterinary clinic, 111(12.1%) young, 548(59.6%) adult and 261(28.4%) were old (Table 1). Concerning the study population, 654(71.1%) cattle, 62(6.7%) chicken, 66(7.2%) goat and 138(15.0%) were sheep in diagnosed food animals (Table 2). Regarding the agro-ecological zones in study area, 542(58.9%), 129(14.0%) and 249(27.1%) of diagnosed animals were highland, lowland and midland respectively (Figure 1). Likewise, 102(53.9%), 6(0.5%), 38(20.1%), 1(0.5%),52(27.5%),16(8.5%),49(25.9%),30(15.9%),6 3.2%) and 8(4.2%) times penstrep was prescribed against Black leg, Bloat, Bovine Mastitis, Dermatophytosis, Lumpy and Skin Disease(LSD) ,Newcastle Diseases(NCD), Pasteurellosis, Pneumonia, Powl typhoid and Salmonellae respectively. Albendazole was also prescribed for the treatment of 14 (6.1%) %) bacterial infection cases (Table 4).All the drugs prescribed between the studies periods were by generic naming. However, most of the drug prescriber’s status was not identified at Ateso veterinary clinic.

Table1: Age category of animals diagnosed

Age category	No. of food animals diagnosed	Percent	Cumulative Percent
Young	111	111(12.1%)	12.1
Adult	548	548(59.6%)	71.6
Old	261	261(28.4%)	100.0
Total	920	920(100.0%)	

Table2: Food Animal species examined during veterinary drug prescription

Types of food animals diagnosed	No. of food animals diagnosed	Percent	Cumulative Percent
Cattle	654	654(71.1%)	71.1
Chicken	62	62(6.7%)	77.8
Goat	66	66(7.2%)	85.0
Sheep	138	138(15.0%)	100.0
Total	920	100(100.0%)	

DOI: 10.47504/IJAGRI.2022.3.4.1

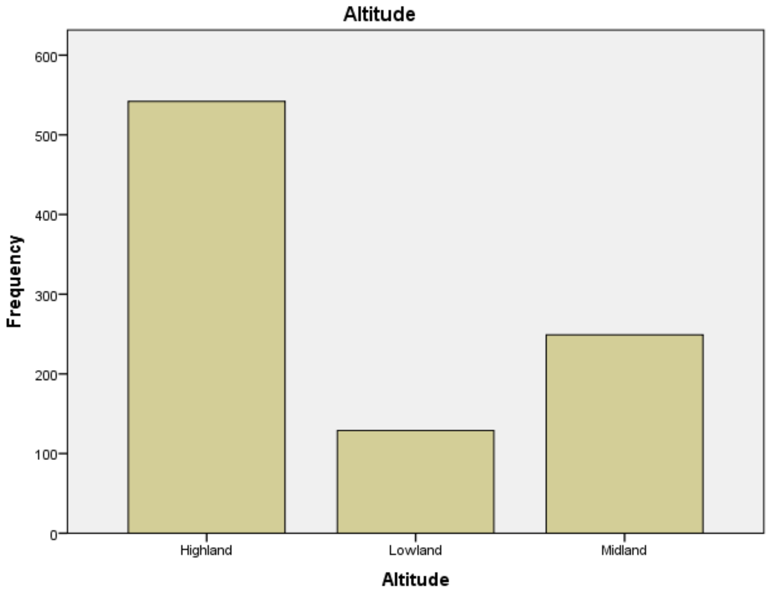

Figure 1: Different agro-ecological zones in study area.

Table 3: Commonly prescribed veterinary drugs in Ateso veterinary clinic

Commonly prescribed veterinary drugs	Total Nnumber (%)	Total
Total drugs	972	972
Oxytetracycline	189(19.4%)	189
Penstrep	308(31.7%)	308
Albendazole	226(23.3%)	226
Isomitamidium chloride	36(3.7%)	36
Ivermectine	120(12.3%)	120
Sulfa drugs	65(6.7%)	65
Veridium	28(2.9%)	28

DOI: 10.47504/IJAGRI.2022.3.4.1

Table 4: Association between diseases and drugs administered at Ateso veterinary clinics.

Disease diagnosed	N (%))	Oxytetracycline	Penstrep	Albendazole	Isomitamidium chloride	Ivermectine	Sulfa drugs	Veridium
Black leg	250(14%)	16(8.5%)	102(53.9 %)	4(1.8%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Bloat	126(7.1%)	2(1.1%)	6(0.5%)	0(0.0)	0(0.0)	0(0.0)	61(93.8 %)	0(0.0)
Bovine Mastitis	94(5.2%)	5(2.6%)	38(20.1%)	1(0.4%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dermatophytosis	247(13.8%)	2(1.1%)	1(0.5%)	95(42%)	1(2.8%)	62(0.0)	0(0.0)	0(0.0)
GIP	261(14.6%)	1(0.5%)	0(0.0)	115(50.9 %)	0(0.0)	58(48.3 %)	0(0.0)	0(0.0)
LSD	131(7.3%)	10(5.3%)	52(27.5%)	2(0.9%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
NCD	50(2.8%)	8(4.2%)	16(8.5%)	0(0.0)	0(0.0)	0(0.0)	1(1.5%)	0(0.0)
Pasteurellosis	370(20.7%)	116(61.4 %)	49(25.9%)	9(3.9%)	1(2.8)	0(0.0)	0(0.0)	0(0.0)
Pneumonia	76(4.2%)	8(4.2%)	30(15.9%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Powl typoid	19(1.1%)	4(2.1%)	6(3.2%)	0(0.0)	0(0.0)	0(0.0)	1(1.5%)	0(0.0)
Salmonellae	54(3.0%0	17(%8.9)	8(4.2%)	0(0.0)	0(0.0)	0(0.0)	2(3.1%)	0(0.0)
Trypanosomosis	130(7.3%)	0(0.0)	0(0.0)	0(0.0)	34(94 %)	0(0.0)	0(0.0)	28
Total	1788	189	308	226	36	120	65	28

Table 5: Association between prescribed drugs and their combinations

Tentative diagnosis	Total count	AB+Sulfa drugs	AH+AH	Total
Black leg	124	0	0	124
Bloat	58	7	0	65
Bovine Mastitis	46	0	0	46
Dermatophytosis	112	0	24	136
GIP	116	0	29	145
LSD	65	0	0	65
NCD	25	0	0	25
Pasteurellosis	174	0	1	175
Pneumonia	38	0	0	38
Powl typoid	10	0	0	10
Salmonellae	27	0	0	27
Trypanosomosis	64	0	0	64
Total	859	7	54	920

6. DISCUSSIONS

Retrospective and cross-sectional study results of drugs used at Ateso clinic of the study sites indicated that a total of 920 animals were presented to the clinics and 1788 drugs were prescribed with an average per case of 1.9 (with the maxi-mum of 2 and a

DOI: 10.47504/IJAGRI.2022.3.4.1

minimum of 1 drug) which is almost equivalent to the World Health Organization (WHO) standard prescription guidelines that range between 1.6 and 1.8. (Isah., *et al*, 2004). A high average number of drug prescriptions might be due to a lack of therapeutic training of prescribers or a shortage of therapeutically correct drugs. However, the low values might show inadequate availability of drugs (Anteneh, 2013).

A national baseline study on drug use indicators (human subjects) in Ethiopia in 2002 also showed that the percentage of encounters in which an antibiotic was prescribed be 58.1% [15], which was nearly equivalent to the current result. Like antibiotics, there were also reports on anthelmintic resistance because of irrational anthelmintic prescription. For instance, resistance to Albendazole and Ivermectin by Cooperia and Haemonchus species was reported in several countries (Anziani., *et al*, Smith and Gasbarre, 2004, 2005).

The basic purpose of veterinary drugs is to protect the health and welfare of animals (Smith and Gasebarre, Riviere and Sundlot, 2005, 2001). However, 4 (0.43%) antibiotics (3 Oxytetracyclines and 1 Penstrep) ($p < 0.005$) were prescribed irrationally to treat diseases that were tentatively diagnosed as parasitic cases (Table 4). The association between antibiotic used and parasitic cases is statistically significant ($p < 0.001$). Such a low level of antibiotic prescription may be accounted for by the assumption that every medical condition will very likely present with less bacterial complication. In addition, 15(1.6%) Albendazole ($p < 0.005$) where prescribed irrationally for cases diagnosed as bacterial and viral infection (Table 4).

Even though all of the cases encountered in the Ateso veterinary clinic received drug therapy after they had been tentatively diagnosed, the route of drug ad- ministration and length of treatment were not indicated for some the prescribed drugs, which revealed the presence of irrational drug use. Such practice of drug prescription (prescription of unnecessary drugs, in- appropriate choice of route, dose, and duration of antibiotics (Pallares., *et al*, 1993) in food-producing animals probably results in drug residues, which may promote allergenic, toxic, mutagenic, teratogenic, or carcinogenic, and it may favor the emergence of resistant microbial strains within a host (Riviere and Sundlof, 2001).

In other ways, from the total of drugs prescribed (1788) at these study sites, Penstrep 308(31.7%) was the most commonly used followed by Albendazole 226(23.3%), Oxytetracycline 189(19.4%), Ivermectine 120 (12.3%), sulfa drugs 65(6.7%), Isomitamidium chloride 36(3.7%) and Veridium 28(2.9%).

However the combination drugs are irrational because of their doubtful stability, reducing the efficacy increases the risk of side effects and may also needlessly increase the cost; 6.3 % of anthelmintics and 0.8 % antibiotics with sulfa drugs were prescribed (Table 5). Combination drugs should be only used when there is no alternative of single drugs available for treatment or no alternative single drug is cost-effective for the purpose. One of the main causes of irrational use of medicines may be the availability of irrational fixed-dose combinations (Kasarla., *et al*, 2013).

7. CONCLUSION AND RECOMMENDATIONS

The pattern of rational drug use at the current study clinic was generally not satisfactory, although the level of generic prescription was recommendable compared to the WHO standards. The study showed that the use of antibiotics and anthelmintic are too high and there may therefore be the need to establish protocols on drug prescription. The overall picture of drug use suggests that the indicators at these facilities are not yet at the optimal level and need some interventions. The result obtained in this study provides a baseline for veterinarians and concerned bodies of the respective districts of the study sites in particular and the country, in general, to monitor and make the necessary educational and managerial interventions to improve the situation in veterinary drugs use. Hence, we suggest corrective measures should be undertaken to facilitate rational drug use in food-producing animals through improving the availability of diagnostic facilities at veterinary clinics to improve patient misdiagnoses and awareness of veterinary clinical practitioners about rational drug use. Further research should also be conducted to evaluate the rational veterinary drug use at different agro-ecologies of the country to take appropriate in general and food animals in particular.

DOI: 10.47504/IJAGRI.2022.3.4.1

REFEREENCE

Anteneh, "Assessment of drug use pattern using WHO prescribing indicators," BMC Health Services Research, vol. 13, p. 170, 2013.

Isah, D. Ross-Degnan, J. Quick, R. Laing, and A. Mabadeje, 2004, The development of standard values for the WHO drug use prescribing indicators," in Proceedings of the International Conference on Improving Use of Medicines (ICIUM). INRUD Nigeria, Support Group; DAP-WHO, pp. 68–72, Abuja, Nigeria, March 2004.

R. Pallares, R. Dick, R. P. Wenzel, J. R. Adams, and M. D. Nettleman, "Trends in antimicrobial utilization at a tertiary teaching hospital during a 15-year period (1978- 1992)," Infection Control & Hospital Epidemiology, vol. 14, no. 7, pp. 376–382, 1993.

O. S. Anziani, V. Suarez, A. A. Guglielmone, O. Warnke, H. Grande, and G. C. Coles, "Resistance to benzimidazole and macrocyclic lactone anthelmintics in cattle nematodes in Argentina," Veterinary Parasitology, vol. 122, no. 4, pp. 303–306, 2004.

L. Smith and L. Gasbarre, "Effect of single or combinational drug treatment on epg values in commercial cattle operation harboring nematode parasites resistant to multiple classes of anthelmintics," in Proceedings of the 50th American Association of Veterinary Parasitologists, pp. 137-138, Minneapolis, MN, USA, July 2005.

Riviere and Sundlof, 2001 J. Riviere and S. Sundlof, "Chemical residue in tissues of food animals," in Veterinary Pharmacology and *erapeutics, H. R. Adams, Ed., pp. 1166–1174, Blackwell Publishing Professional, Iowa, IA, USA, 8th edition, 2001.

Biswas, 2003 S. Biswas Role of veterinarians in the care and management during harvest of skin in livestock species Proc. National Seminar on Leather Industry in Today's Perspective, Kolkata, India (2003), pp. 62-64

FAO, 1984 FAO Tick-borne diseases control, Vol. 1 (1984) Rome http://www.niaid.nih.gov/topics/tickborne/Pages/Default.aspx

Ghosh, P. Azhahianambi, M.P. Yadav Upcoming and future strategies of tick control: a review J. Vect. Borne Dis, 44 (2007), pp. 79-89 View Record in ScopusGoogle Scholar

Jongejan and Uilenberg, 1994 F. Jongejan, G. Uilenberg Ticks and control methods J. Blancou (Ed.), Ectoparasites of animals and control methods, Sci Tech Rev, 13 (4), Office Internationale des Epizooties (OIE), Paris, France (1994), pp. 1201-1226

Martins et al., 1995 J.R. Martins, B.L. Correa, V.H. Cereser, C.C.P. Arteche A situation report on resistance to acaricides by the cattle tick *Boophilus microplus* in the State of Rio Grande does Sul, Southern Brazil C.S. Rodriguez, S.H. Fragosso (Eds.), Resistencia y Control en Garrapatas y Moscas de Importancia Veterinaria 111 (1995)

Abdulahi M, Shiferaw T (1997) Pattern of prescription in Jimma Hospital.Ethiop J Health Dev 11: 263-267.

Abraham E. (1987). Cephalosporins. Drugs. 4(2):1 -4

Adzitey F. (2015). Antibiotic classes and antibiotic susceptibility of bacterial isolates from selected poultry; a mini-review. World Vet. J. 5 (3):36-41.

Akhter, N., Lal, C., Gadahi, J.A., Mirbahar, K.B. and Memon, M.I., 2010. Efficacy of various antiprotozoal drugs on bovine babesiosis, anaplasmosis, and theileriosis. Veterinary World, 3(6), p.272.

Amane, H. and Kop, P., 2011. Prescription analysis to evaluate the rational use of antimicrobials. *Int J Pharmacol Biol Sci*, *2*(2), pp.314-9.

Barbosa J, Cruz C, Martins J, Silva JM, Neves C, et al. (2005) Food poisoning by clenbuterol in Portugal. Food Addit Contam 22: 563-566.

Beyene, T., Endalamaw, D., Tolossa, Y. and Feyisa, A., 2015. Evaluation of rational use of veterinary drugs especially antimicrobials and anthelmintics in Bishoftu, Central Ethiopia. BMC research notes, 8(1), pp.1-8.

Boundless (2016). Antibiotic Classifications. Boundless microbiology. https://www.boundless.com/microbiology/textbooks/boundlessmicrobiology-textbook/antimicrobial-drugs-13/overview-ofantimicrobial-therapy-153/antibiotic-classifications-775-4905/. Accessed September 13, 2016

Bush, K., and Bradford, P.A., 2016. B-Lactams and β-lactamase inhibitors: an overview. Cold Spring Harbor perspectives in medicine, 6(8), p.a025247.

Calderon C. B. & Sabundayo B. P. (2007). Antimicrobial classifications: Drugs for bugs. In: Schwalbe R, Steele-Moore L & Goodwin AC (eds). Antimicrobial susceptibility testing protocols. CRC Press, Taylor and Frances group. ISBN 978-0-8247-4100-6

Cheesman, S.J., 2000. The topoisomerases of protozoan parasites. Parasitology Today, 16(7), pp.277-281.

Choquet-Kastylevsky G., Vial T. & Descotes J. (2002). Allergic adverse reactions to sulfonamides. Curr. Allergy Asthma Rep. 2(1):16-25.

DOI: 10.47504/IJAGRI.2022.3.4.1

Crawford, A. M., Paterson, K. A., Dodds, K. G., Tascon, C. D., Williamson, P. A., Thomson, M. R., Bisset, S. A., Beattie, A. E., Greer, G. J., and Green, R. S. (2006). Discovery of quantitative trait loci for resistance to parasitic nematode infection in sheep: I. Analysis of outcross pedigrees. *BMC genomics* **7**, 178

Cully, D. F., Vassilatis, D. K., Liu, K. K., Paress, P. S., Van der Ploeg, L. H., Schaeffer, J. M., and Arena, J. P. (1994). Cloning of an avermectin-sensitive glutamate-gated chloride channel from Caenorhabditis elegans. *Nature* **371**, 707-711.

DACA (2006) Standard treatment guidelines for veterinary practice. (1stedn) Drug administration and control authority of Ethiopia, Addis Ababa, Ethiopia:

Endale, G., Solomon, A., Wuletaw, A. and Asrat, A., 2013. The antibiotic prescribing pattern in a referral hospital in Ethiopia. *African Journal of Pharmacy and Pharmacology*, *7*(38), pp.2657-2661.

Endale, G., Solomon, A., Wuletaw, A. and Asrat, A., 2013. The antibiotic prescribing pattern in a referral hospital in Ethiopia. *African Journal of Pharmacy and Pharmacology*, *7*(38), pp.2657-2661.

European medicines agency (2004). "Veterinary medicines and inspections. Committee for medicinal products for veterinary use." European medicines agency.

Eyssen H. J., Van den Bosch J. F., Janssen G. A. & Vanderhaeghe H. (1971). Specific inhibition of cholesterol absorption by sulfaguanidine. Atherosclerosis. 14 (2):181 -192.

Frank U. & Tacconelli E. (2012). The Daschner Guide to In-Hospital Antibiotic Therapy. European standards. Available online at: http://www.springer.com/978-3-642-18401 -7. 300p.

Fuoco D. (2012). Classification framework and chemical biology of tetracycline-structure-based drugs. Antibiotics. 1:1 -13.

Gasbarre, L.C., Smith, L.L., Lichtenfels, J.R. and Pilitt, P.A., 2009. The identification of cattle nematode parasites resistant to multiple classes of anthelmintics in a commercial cattle population in the US. *Veterinary parasitology*, *166*(3-4), pp.281-285.

Geary TG, Woo K, McCarthy JS, Mackenzie CD, Horton J, et al. (2010) Unresolved issues in anthelmintic pharmacology for helminthiases of humans. Int J Parasitol 40: 1-13.

Gilbert D. (2000). Aminoglycosides. In: Mandell G. L., Bennett J. E. & Dolin R, (eds.) Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 5th ed. Philadelphia: Churchill Livingstone. Pp. 307-336

Hennessy, D., and Alvinerie, M. (2002). Pharmacokinetics of the macrocyclic lactones: conventional wisdom and new paradigms. *Macrocyclic lactones in antiparasitic therapy* **97**, 124.

Henry R. J. (1943). The mode of action of sulfonamides. Bacteriol. Rev. 7(4):175-262.

Köhler, P. (2001). The biochemical basis of anthelmintic action and resistance. Elsevier.

Laing R, Hogerzeil H, Ross-Degnan D (2001) Ten recommendations to improve the use of medicines in developing countries. Health Policy Plan 16:13-20.

Laing, R.O., Hogerzeil, H.V. and Ross-Degnan, D., 2001. Ten recommendations to improve the use of medicines in developing countries. *Health policy and planning*, *16*(1), pp.13-20.

Leathwick, D., and Miller, C. (2013). Efficacy of oral, injectable, and pour-on formulations of moxidectin against gastrointestinal nematodes in cattle in New Zealand.*Veterinary Parasitology* **191**, 293-300.

Mahajan G. B. & Balachandran L. (2012). Antibacterial agents from actinomycetes - a review. Front Biosci. (Elite Ed). 4:240-253.

Matter D, Rossano A, Limat S (2007) Antimicrobial resistance profile on actinobacillus pleuropneumoniae and actinobacillus porcitonsillarum.Vet microbial 122: 144-156.

McGeer A., Fleming C. A., Gree K. & Low D. E. (2001). Antimicrobial resistance in Ontario: Are we making progress? Laboratory Proficiency Testing Program Newsletter.293:1 -2.

Medical News Today (2015). Antibiotics: How do antibiotics work? MediLexicon International Ltd. Bexhill-on-sea UK

Merck Veterinary Manual (2008). A Handbook of Diagnosis, Therapy, and Disease Prevention and Control for the Veterinarian. Merck & Co. *In* "Whitehouse Station", NJ,USA Inc.

Nagawade, R. R., and Shinde, D. B. (2006). BF~ 3· OEt~ 2 promoted solvent-free synthesis of benzimidazole derivatives. *Chinese Chemical Letters* **17**, 453.

Nasir, A.A., 2000. Effects of theileriosis on blood parameters of exotic cattle and efficacy of buparvaquone and oxytetracycline. Pakistan Journal of Biological Sciences (Pakistan).

Pegler S. & Healy B. (2007). In patients allergic to penicillin, consider second and third-generation cephalosporins for life-threatening infections. BMJ. 335(7627): 991.

Prichard, R. (2005). Is anthelmintic resistance a concern for heartworm control?: What can we learn from the human filariasis control programs? *Veterinary Parasitology* **133**, 243-253.

Rehan HS, Singh C, Tripathi CD, Kela AK (2001) Study of drug utilization pattern in dental OPD at a tertiary care teaching hospital. Indian J Dent Res 12: 51-56.

Sanchez A. R., Rogers R. S. & Sheridan P. J. (2004). Tetracycline and another tetracycline-derivative staining of the teeth and oral cavity. Int.J. Dermatol. 43(10):709-715.

DOI: 10.47504/IJAGRI.2022.3.4.1

Sanders P (2007) Veterinary drug residue control in the European Union.Technologija mesa 1: 59-68.

Slatore C. G. & Tilles S. A. (2004). Sulfonamide hypersensitivity. Immunol. Allergy Clin. North Am. 24(3):477-490.

Soulsby EJ (2005) Resistance to antimicrobials in humans and animals.BMJ 331: 1219-1220.

Soulsby, E.J.L., 1982. Helminths. Arthropods and Protozoa of domesticated animals, 291.

Stawinski J., Szafranski K., Vullo D. & Supuran C. T. (2013). Carbonic anhydrase inhibitors. Synthesis of heterocyclic 4-substituted pyridine-3-sulfonamide derivatives and their inhibition of the human cytosolic isozymes I and II and transmembrane tumor-associated isozymes IX and XII. Eur. J. Med. Chem. 69:701 -710.

Stepek, G., Behnke, J. M., Buttle, D. J., and Duce, I. R. (2004). Natural plant cysteine proteinases as anthelmintics? TRENDS in Parasitology 20, 322-327.

Talaro K. P. & Chess B. (2008). Foundations in microbiology. 8th Ed. McGraw Hill, New York.

Talaro K. P. & Chess B. (2008). Foundations in microbiology. 8th Ed. McGraw Hill, New York.

Urquhart, G.M., J.Armour, J.L.Duncan, A.M.Dunn and F.W. Janings. (1988) Vet. Parasitol. Ist Ed: ELBS, Longman, London, UK.

Van Hoek A. H. A. M., Mevius D., Guerra B., Mullany P., Roberts A. P. & Aarts H. J. M. (2011). Acquired antibiotic resistance genes: An overview. Front. Microbiol. 2:203 doi: 10.3389/fmicb.2011.00203.

Vitomir C, Silva D, Biljana A, Sanja C (2011) the significance of rational use of drugs in veterinary medicine for food safety. Tehnologija mesa 52:74-79.

VMD (2008) Assuring the safety, quality, and efficacy of veterinary drugs. Sales of antimicrobial products for use as veterinary medicines, antiprotozoals, antifungals, growth promoters, and coccidiostats in the UK in 2007, UK.

WHO (1993) World Health Organization. How to investigate drug use in health facilities: selected drug use indicators. WHO, Geneva. WHO (2012) rational use of medicines. World Health Organization.

World Health Organization, 1993. *How to investigate drug use in health facilities: selected drug use indicators* (No. WHO/DAP/93.1 Unpublished). World Health Organization.

World Health Organization, 2003. *Assessment of the pharmaceutical sector in Ethiopia* (No. TODOC). Addis Ababa, Ethiopia.: Ministry of Health.

Xia, J., Gao, J. and Tang, W., 2016. Nosocomial infection and its molecular mechanisms of antibiotic resistance. Bioscience trends, 10(1), pp.14-21.

Xu F., Xu H., Wang X., Zhang L., Wen Q., Zhang Y. & Xu W. (2014). Discovery of N-(3-(7H-purin-6-yl)thio)-4-hydroxy naphthalene-1 -yl)- sulfonamide derivatives as novel protein kinase and angiogenesis inhibitors for the treatment of cancer: synthesis and biological evaluation. Part III. Bioorg. Med. Chem. 22(4):1487-1495.

Zahner H. & Maas W. (1972). Biology of Antibiotics. Springer-Verlag, New York.

Zajac, A. M. (2006). Gastrointestinal nematodes of small ruminants: life cycle, anthelmintics, and diagnosis. *Veterinary Clinics: Food Animal Practice* **22**, 529- 541.

R. Kasarla, A. Elumalai, and S. Eddla, "Irrational drug combinations," International Journal of Experimental Pharmacology, vol. 55, 2013.

DOI: 10.47504/IJAGRI.2022.3.4.1