Antiprotozoal drugs:-Anticoccidial drug :-

1-Sulfonamides.
2-Nitrofurans.
3-Thiamine antagonist(Amprolium, Diaveridine, Ethopabate).
4-Quinolates.
5-Robenidine.
6-Aprinocid.

Sulfonamide:-

Sulphonamides: They have longest history of use as anticoccidial drugs. The common drugs of this group which are used as anticoccidials are sulphadimidine, sulphaquinoxaline, sulphadimethoxine, sulphanitran and sulphaguanidine. Sulphonamides have broad spectrum of activity against eimerian species and have coccidiostatic action. They are used for prevention and treatment of coccidia and in outbreaks. They are more effective against intestinal than caecal forms of coccidia. They stop the onset of the disease by acting against the second generation schizonts of E. tenella and E. necatrix. They can act upon first generation schizonts and possibly against sexual stages but much higher doses are required. Use of these drugs does not impair immunity development.

Mechanism of action: mechanism of action of sulphonamides, coccidian is synthesizing their own folic acid utilizing PABA (p-amino-benzoic acid) from growing medium because folic acid is required for growth/replication of DNA. Sulfonamides are structural analogues (PABA and Sulfonamide is similar in nature) of PABA inhibit bacterial folate synthetase resulting into folic acid is not formed and a number of essential metabolic reactions suffer. Animal cells also require folic acid but they utilize performed folic acid supplied in diet and are unaffected by sulfonamides. Therefore they prevent proper development of schizonts. Diaminopyrimidines inhibits the conversion of folic acid to tetrahydrofolic acid and are used in combination with Sulphonamides to potentiate their anticoccidial action.

Nitrofurans:-

Thiamine antagonist:- Amprolium:

it is quarternized derivative of pyrimidine which is a thiamine antagonist. It is most active against *E. tenella, E. necatrix* and *E. acervulina* and to lesser extent *E. maxima*. Combination of amprolium with ethopabate, sulphaquinoxaline or even pyrimethamine extended and strengthened the spectrum of activity. It could be fed at several times the recommended dose with no ill effects and probably, one of the safest antimicrobial drugs to be used extensively. It is effective against 1st generation of trophozoites and schizonts and shows peak activity early in day 3 of cycle. It also suppresses the sexual stages, gametogony and sporulation of oocyst. Continuous use of Amprolium is resulting into the development of drug resistance which is a major problem and limiting its use. It is rarely used alone because *E. maxima* and other species are resistant and therefore given in combination with other drugs. Amprolium is available as a premix and is given prophylactically to birds in a final concentration of 0.0125 percent. In combination with 2 other drugs, it is given at a level of 0.006% of each in the food with better effectiveness[6]. A combination of amprolium and sulphaquinoxaline at levels of 0.006% of each in the food is more effective against poultry coccidiosis than either of the two drugs used alone[7]. There is no premarketing withdrawal requirement for this compound. Amprolium is compatible with vitamins, antibiotics, minerals and other ingredients commonly used in poultry ration but it should not be mixed in concentrates containing high levels of choline because of tendency for it to break down into picric acid.

Mechanism of action: It is thiamine antagonist and due to its close structural similarity it blocks the thiamine receptors. This blockage of receptors prevents coccidia from utilizing thiamine and as a result thiamine is unavailable to coccidian. This vitamin (thiamine pyrophosphate) is a cofactor of several decarboxylase enzymes which play role in cofactor synthesis. It is only agent which can be used in laying birds both for prevention and treatment of outbreaks. At higher doses, thiamine deficiency can occur in host but it can be prevented by addition of thiamine.

Buquinolate: It has broad spectrum of activity against all chicken decoquinate and nequinate are the examples of Quinolones which have shown great efficacy against all species of poultry coccidia. Quinolones have limited absorption because they are virtually insoluble in water. Tissue residues of Quinolones are very low and the liver is the main organ which has greatest concentration. They act on the sporozoite stage of the life cycle of coccidian. The sporozoite is evidently able to penetrate the host intestinal cell but its further development is prevented. Thus on day 1st of life cycle, these compounds show maximum activity. So, these

drugs must be in feed on day one of exposure to coccidia to give maximum advantages.

Mechanism of action: Anticoccidial activity of these compounds depends on disruption of electron transport in cytochrome system of mitochondria in coccidia while decoquinate inhibits DNA synthesis by inhibiting DNA gyrase and not effective in treatment of clinical coccidiosis. Quinolones is a class of anticoccidials which is not able to give complete control of oocyst production. The compounds of this class are not able to completely eliminate the oocyst which enhances the potential for the development of drug resistant strains of coccidia. Thus their use in chicken as anticoccidials is now limited.

Robenidine : It is a broad spectrum coccidiostatic and coccidiocidal drug, used for the prophylaxis of coccidiosis. Robenidine is approved for use in chickens to prevent outbreaks of coccidiosis. It is effective against all *Eimeria* species.

Mechanism of action. The mechanism of action is undetermined. Its Peak activity is on the first generation schizonts. **It inhibits oxidative phosphorylation in late first generation and second stage schizonts. It may also have an effect on the gametocytes. It is most effective against the maturing first generation schizonts**

Note:-

It is not used in laying hens and has 5 day withdrawal period for the slaughter of poultry. It imparts unpleasant taste to the flesh of broiler birds if not withdrawn for 5 days

Adverse effects. Robenidine imparts an unpleasant taste to the flesh of broilers, if therapy is not terminated 5 days before slaughter. The taste is imparted to eggs when birds are fed at dosages equal to or greater than 66 ppm.

Aprinocid.

Drugs for treatment of giardiasis:-

1-Metronidazole (Flagyl R)

Chemistry. A nitroimidazole antiprotozoal and antibacterial agent, metronidazole is lipophilic.

Mechanism of action. A ferrodoxin-linked metabolite of metronidazole disrupts DNA synthesis in protozoans and bacteria.

Therapeutic uses. Metronidazole is a broad-spectrum antiprotozoal drug that is effective against giardia, histomonas, babesia, trichomonas, and *ameba*. It is approved as a human drug, and has been used largely in small animals

Pharmacokinetics
a. Absorption. The oral bioavailability of metronidazole in animals varies 50–100%.
If given in food, absorption is enhanced, attributable to increased bile secretion that helps dissolve metronidazole. Peak blood levels occur within 1 hour of administration.

b. Distribution. Metronidazole is rapidly and widely distributed after oral absorption, because it is highly lipophilic
.
c. Metabolism and excretion. Metronidazole undergoes hydroxylation and conjugation in the liver.
Both metabolites and parent drug are eliminated in the urine and feces in 24 hours. The elimination *t*1/2 is 4–5 hours in dogs.

Adverse effects. High doses of metronidazole or prolonged administration may induce lethargy, weakness, ataxia, rigidity, anorexia, vomiting, diarrhea, reversible leukopenia, and hepatotoxicity. Because metronidazole affects DNA synthesis, it may have teratogenic and carcinogenic effects.

Other drugs for treatment of giardiasis—Albendazole and fenbendazole

Albendazole may be toxic to liver and bone marrow and is a teratogen.

Antibabesial Drugs:-

1-Quinuronium sulphate

2-Amicarbalide

3-Imidocarb.

4-Diminazene.

5-Suramine.

Drug for treatment of babesiosis in dogs(Imidocarb (Imizol R _)

Chemistry. Imidocarb is a diamidine derivative.
Mechanism of action. Imidocarb binds to DNA and interfere with parasite replication.
Therapeutic uses. Imidocarb is effective against *Babesia canis* when given at a single dose of 6.6 mg/kg IM or SC. Repeat the dose in 2 weeks. Imidocarb eliminates equine babesia (*B. caballi*) when given 1–2 mg/kg, twice during a 24-hour period.
Although effective against bovine babesiosis, imidocarb should not be given to this species because the withdrawal times have not been determined. Feline babesiosis is refractory to imidocab treatment.

a. Adverse effects commonly seen are pain during injection and signs of parasympathetic stimulation such as salivation, nasal drip, or brief episodes of vomiting.
Other effects seen less frequently are panting, restlessness, diarrhea, and injection site inflammation lasting one to several days. Atropine sulfate can be used to control the signs of parasympathetic stimulation.
b. Imidocarb is a teratogen and carcinogen, since it affects DNA synthesis. Do not use in pregnant animals.

Diminazene.

Suramine.

Antitoxoplasmosis drug:-

Sulfonamide ,and trimethoprim ,Clindamycin and Clathromycin

Drugs for treatment of toxoplasmosis

1. Trimethoprim-sulfadiazine, 15 mg/kg, PO, twice a day for 4 weeks.
2. Pyrimethamine (0.25–0.5 mg/kg) plus **sulfadiazine** (30 mg/kg), PO, twice a day for4 weeks.
3. Clindamycin, 10–20 mg/kg, PO or IM, twice a day for 3–6 weeks.

F. Drugs for the treatment of cryptosporidiosis
1. Paromomycin (Humatin R _). Paromomycin is an aminoglycoside for extra-label use;
it can be very expensive.
a. Administration. It can prevent and treat cryptosporidiosis at 50 mg/kg, PO, twice
a day for 10 days.

b. Pharmacokinetics. No information is available for animals. However, GI absorption
after oral administration is minimal, since it is an aminoglycoside.
c. Adverse effects. Paromomycin induces vomiting, diarrhea, colic, renal toxicity,
and deafness.
2. Azithromycin (Zithromax R _ , 15 mg/kg, PO, twice a day for ≥7 days).

3. Nitazoxanide in used in humans for the treatment of cryptosporidiosis.

Anti- theileriosis Drugs :-

Chlorotetracycline and Oxytetracycline, Hydroxynapthoquinone ,Gloxanane.

Antitrypanosomal drugs :-

Quinapyramine, Phenanthridinium compound ,Diminazine ,Suramine.

Antitrichomonal drug :- Nitroimidazole derivatives.

Antihistomoniasis drugs;Dimetridazole.