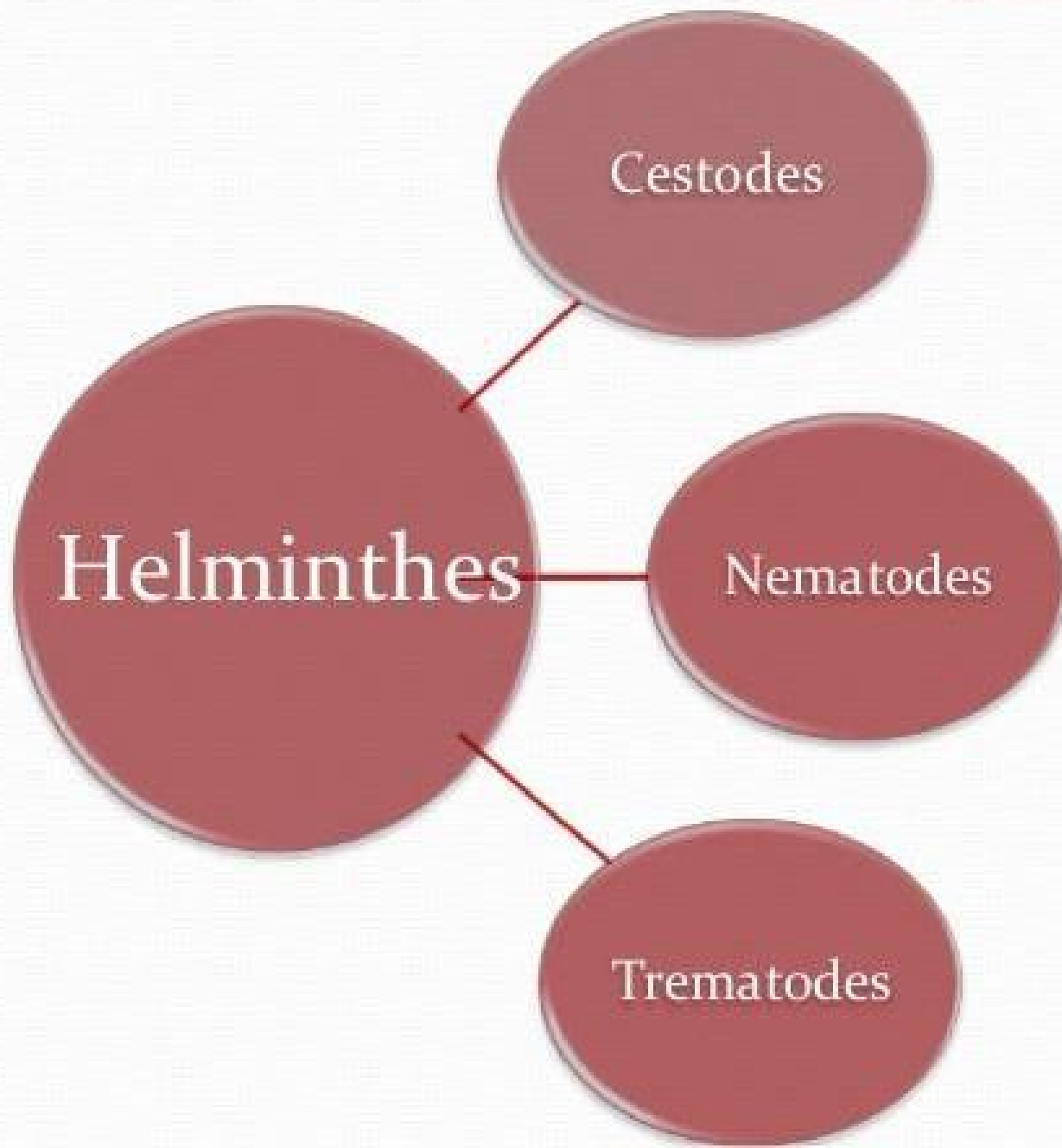


Anthelmintic Drugs

By
Dr. Selamawit Fantahun





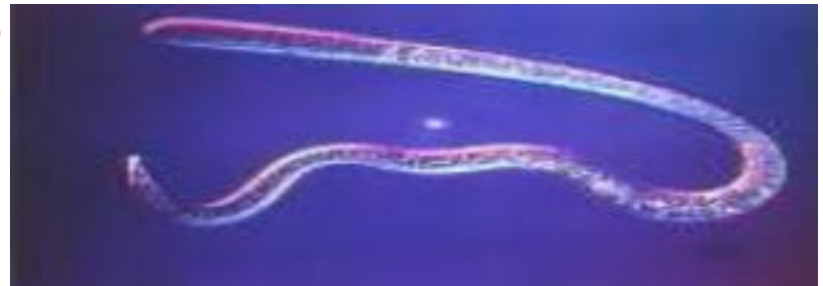
1- INTESTINAL ROUND WORMS (NEMATODES)

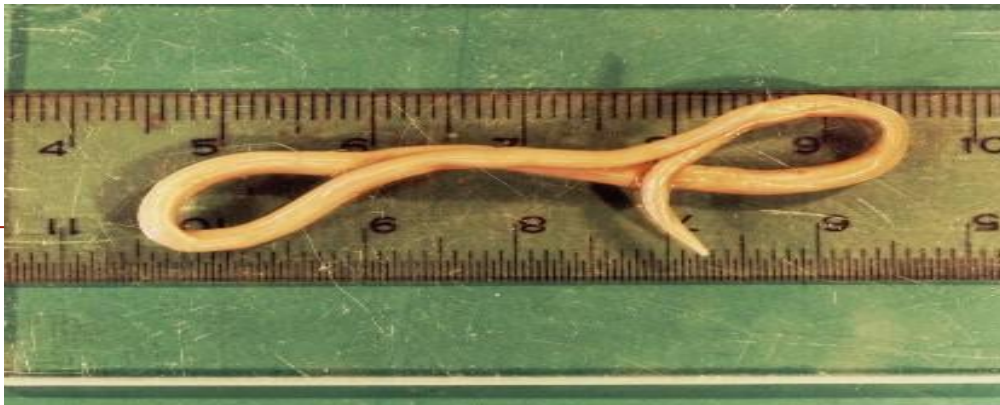
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- **Ascaris Imubricods** (**common round worm**)
- **Enterobius vermicularis** (**pin worm**)
- **Trichuris trichuria** (**whip worm**)
- **Strongyloids stercoralis** (**thread worm**)
- **Ankylostoma duodenale** (**hook worm**)

. TISSUE ROUND WORMS

Trichinella spiralis





Ascaris lumbricoides (common round worm)

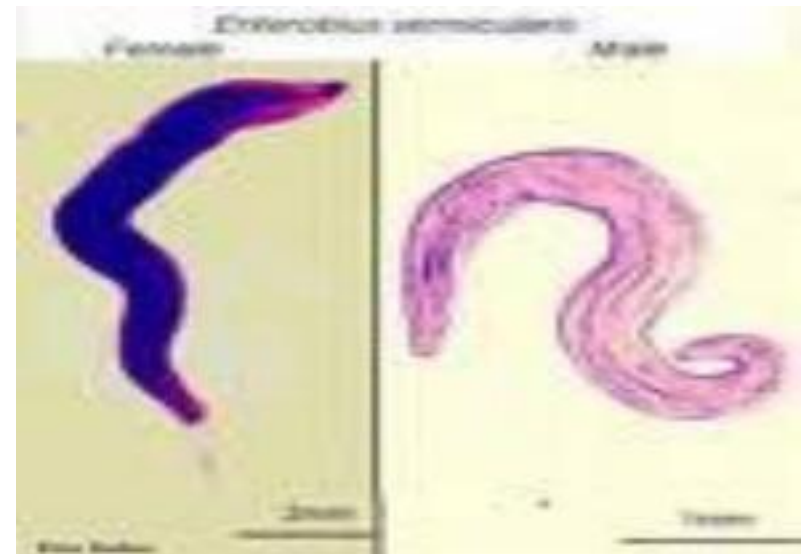


Ancylostoma duodenale

Whipworm



Tricuris tricura



Pinworm male ,female

2. tapeworms (Cestodes)

T. saginata (Beef tapeworm)

T. solium (Pork tapeworm)

Diphyllobothrium latum (fish tapeworm)

In case of *D. latum*
infections by eating raw or
undercooked fish

In some conditions this
larvae may develop causing
cysticercosis (i.e. larvae
gets encysted in muscle , or
more seriously in brain or

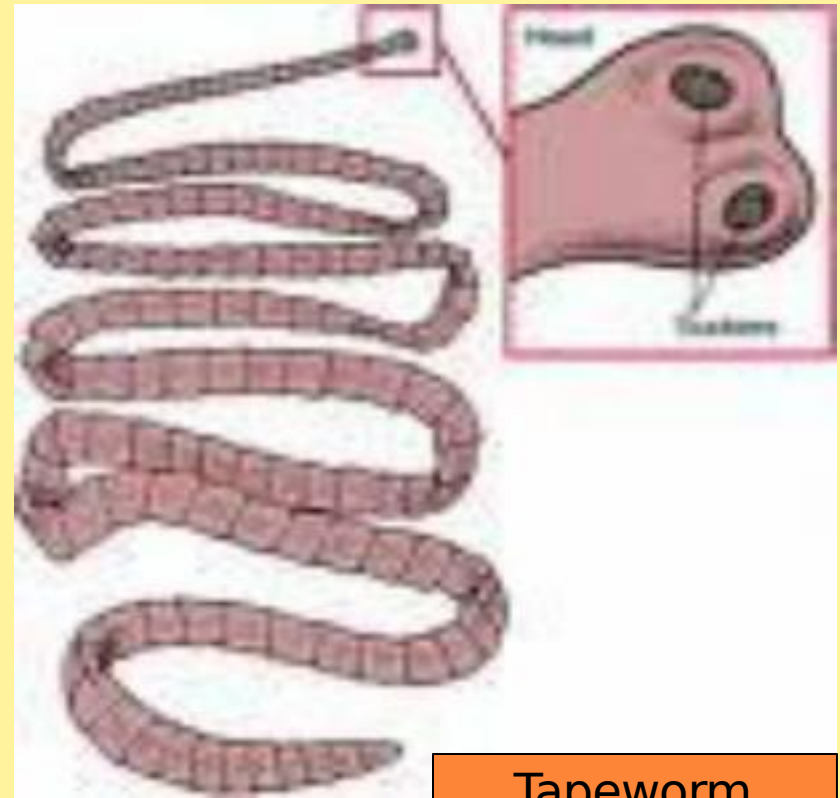


Table 1 : Tapeworms in Small Animals

Cestode	Definitive Host	Comments	Approved Treatments
<i>Dipylidium caninum</i>	Dog, cat	most common tapeworm of dogs , cats	Praziquantel
<i>Taenia taeniaeformis</i>	Cat	Common cestode of cats, rare in dogs	praziquantel, fenbendazole
<i>Taenia hydatigena</i>	Dog	In farm dogs	praziquantel, fenbendazole

TREMATODES (Schistosomes,

FLUKES)

Schistosoma → **SCHISTASOMIASIS** ,
BILHARZIA

**Flukes(Leaf
Like)**



Fasciola hepatica

Lung fluke

Table 2: Commonly Helminths infestation

Cestodes(tapeworms) Intestinal adult worms	Taenia saginata Taenia solium Diphyllobothrium latum	Beef tapeworm Pork tapeworm Fish tapeworm
Larval tissue cysts	Taenia solium Echinococcus granulosus	Cysticercosis Hydatid disease
Nematodes(round worm) Tissue worms Intestinal nematodes	Enterobius vermicularis Ascaris lumbricoides Trichuris trichiura Ancylostoma duodenale Strongyloides stercoralis	Filariasis pin worms Round worms Whipworm Hookworm
Trematodes (flukes) Blood flukes Intestinal / hepatic flukes Lung flukes	Schistosoma species Fasciola hepatica Fasciola gigantica	Schistosomiasis

Anthelmintic Drugs



Anti : against & helminthes : worms

**Drugs kill or expel the internal parasitic
worms infesting GIT & other tissues of man and
animals**

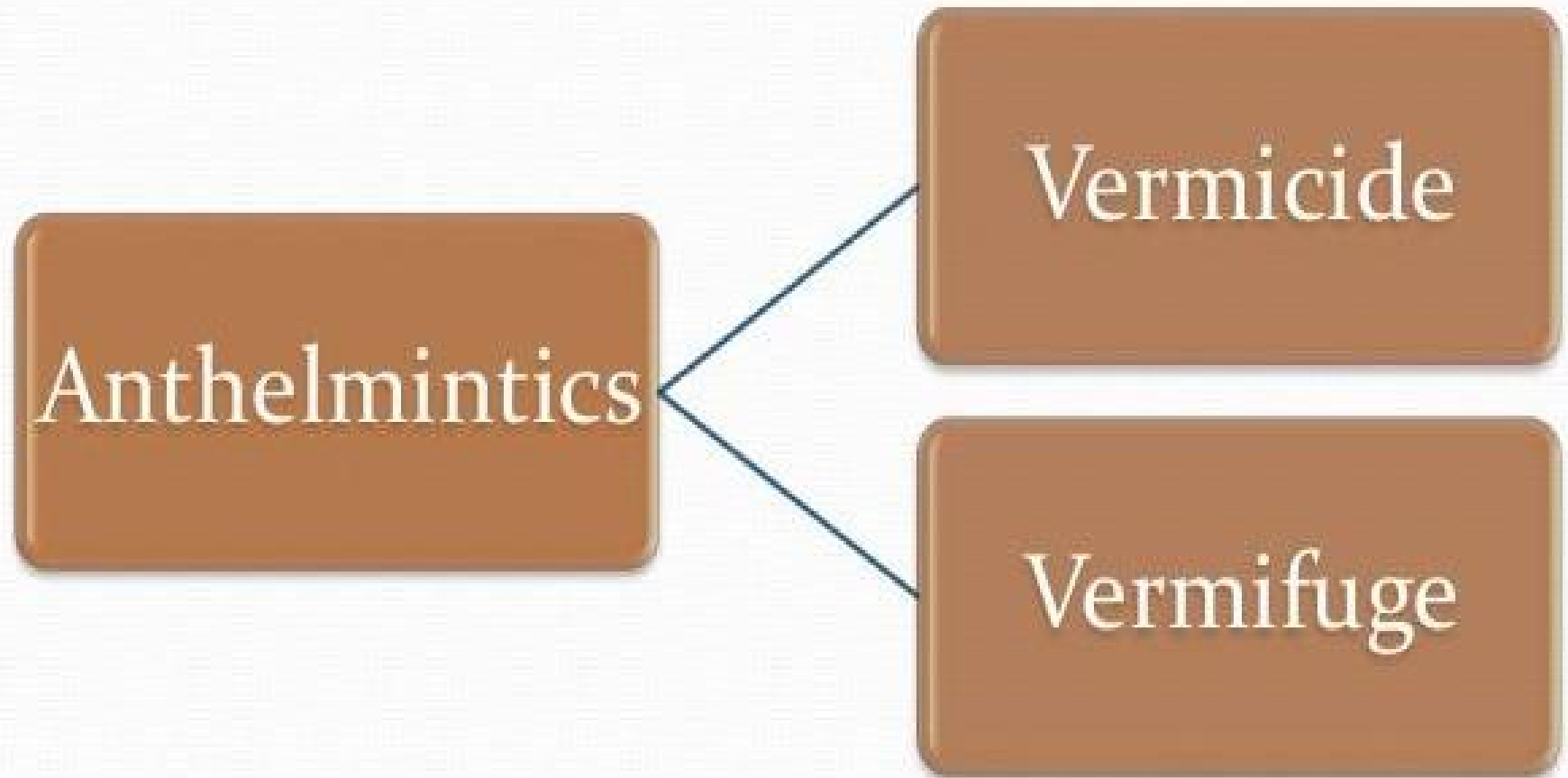
Ideal Anthelmintic drug:

1. A wide therapeutic index; Wide safety margin with highest toxicity to worms, but lesser toxic to the host
- 2- Broad spectrum of activity against mature & immature larval worms of most types of parasites .

Ideal Anthelmintic drug



- 3- Easily administered to animal and have a pleasant taste.
- 4- Effective Orally .
- 5. Effective in a single dose
- 6. Leave no or low tissue residues & have a short residence time in milk when used for treating food producing animals.
- 7 Economic (inexpensive) and compatible with other drugs.



Classification of Anthelmintics



According to the type of action:

Vermicide: Drugs that kill worms(**Bunamidine, Praziquantel**)

Vermifuge : Expel infesting worms alive (**Piperazine**)

According to the spectrum of activity:

Narrow spectrum Anthelmintics

Broad spectrum Anthelmintics

Endectocides

Broad spectrum Anthelmintics :

Active against GI nematodes , tape worms and / or flukes,such as

Benzimidazoles (Thiabendazole, Albendazole & Mebendazole)

Organophosphates (Dichlorvos & Trichlorphon) .

Tetrahydropyrimidines (Morantel and Pyrantel)

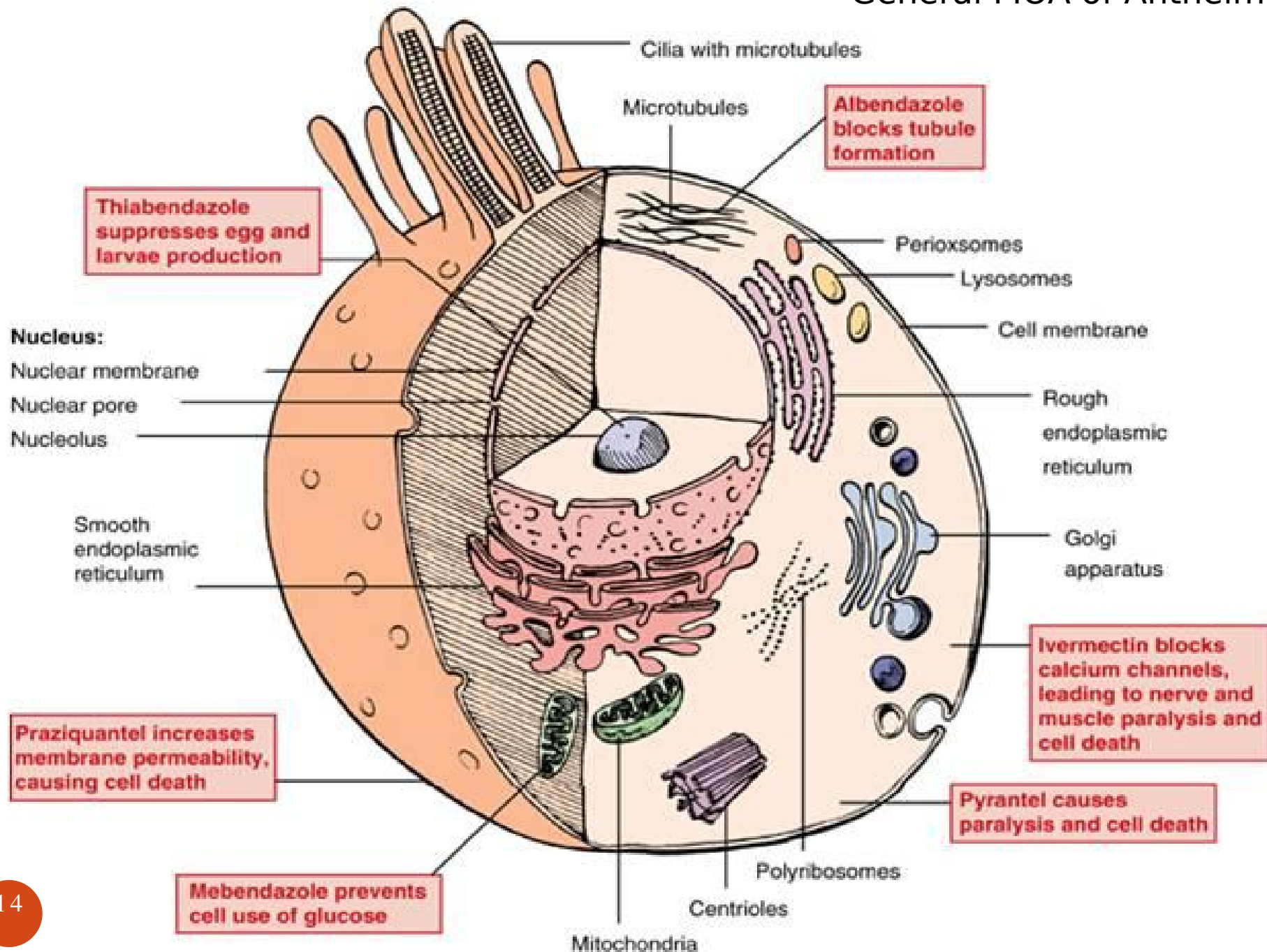
Endectocides:

Drugs effective against both arthropodes & nematodes as both:

Avermectins (Ivermectin) and

According to the type of worms:

Anticestodals - Antinematodals - Antitrematodals



BENZIMIDAZOLES

Several benzimidazoles are in use for the treatment of helminthic infections. Three of these, mebendazole, thiabendazole and albendazole.

They have a broad range of activity against many nematode and cestode parasites, including cutaneous larva migrans, trichinosis, disseminated strongyloidiasis, and visceral larva migrans.

A fourth, triclabendazole, is considered as the drug of choice for *Fasciola hepatica* therapy.

Cont...

Benzimidazoles such as **albendazole**, **fenbendazole**, **flubendazole**, **mebendazole**, **oxfendazole**, **oxibendazole** and **thiabendazole** have a similar mode of action.

Most benzimidazoles are effective against larval and adult roundworms, and albendazole, mebendazole, fenbendazole, oxfendazole, and oxibendazole are also ovicidal.

Triclabendazole is effective against both immature and adult flukes.

Cont...

Most available anthelmintic drugs exert their antiparasitic effects by interference with (1) energy metabolism, (2) neuromuscular coordination, (3) microtubular function, and (4) cellular permeability.

1.MEBENDAZOLE(Vermox)

The immobilizing and lethal action of mebendazole on worms is rather slow; takes 2-3 days to develop.

Mebendazole is one of the preferred drugs for treatment multiples infestations and is more effective than albendazole in trichuriasis, but need for multiple doses are a draw back.

Cont...

It is a synthetic benzimidazole

It has wider spectrum and is more safer than albendazole

Mechanism of action:

It inhibits microtubule synthesis in nematodes that irreversibly impairs glucose uptake. Intestinal parasites are immobilized and die slowly.

It kills hook worm, pin worm , ascariasis and trichuris eggs.

Mebendazole con't

Pharmacokinetics:

Absorption increases with fatty meal.

Absorbed drug is 90 % protein bound

It is converted to inactive metabolites rapidly in liver.

It is primarily excreted in urine.

Cont...

Indications. Gastro-intestinal roundworms in horses, donkeys and sheep; lungworms in donkeys and sheep; tapeworms in sheep

Contra-indications. Administration during first 4 months

of pregnancy, Mebendazole is contraindicated in patients with known hypersensitivity.

Side-effects. Occasional mild diarrhoea

Horses: roundworms, 5–10 mg/kg

Donkeys: Dictyocaulus arnfieldi, 15–20 mg/kg daily

2.ALBENDAZOLE

Albendazole has a broad spectrum of activity against intestinal nematodes and cestodes, as well as the liver flukes.

It is a drug of choice (primary therapeutic application) for treatment of **hydatid disease** and **cystecercosis**, it is also used for the treatment of (**intestinal nematodes**) ascariasis ,tricurasis and strongyloidiasis , pinworm, hookworm.

It also is effective in treating cerebral and spinal neurocysticercosis, particularly when given with

Albendazole cont...

Mechanism of action: It inhibits microtubule synthesis in nematodes(intestinal round worms) that irreversibly impairs glucose uptake, intestinal parasites are immobilized and die slowly.

It is larvicidal in hydatid ,cysticercosis , ascariasis and hook worm infection.

Also ovicidal in ascariasis ,

Pharmacokinetics (Albendazole)

absorption can be increased with fatty meal

It is metabolized in the liver rapidly to active metabolite albendazole

sulphoxide. Sulphoxide is distributed well to tissues, CSF, hydrated cyst

Metabolites are excreted in urine

AND INTERACTIONS

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

Albendazole is contraindicated in patients with known hypersensitivity to the drug and during pregnancy.

Albendazole is used cautiously in patients with hepatic impairment .

It was the first benzimidazole which covered practically all species of nematodes infesting the GIT like round worm, hook worm, Enterobius, Trichris, Strongyloides and Trichinella spiralis.

It also inhibits development of the eggs of worms and kills larvae.

Thiabendazole afford symptomatic relief in cutaneous larvea migrans and skeletal muscle symptoms produced by migration of Trichinella spiralis larvae to muscles.

Cont...

Mechanism Of Action Similar to other benzimidazoles.

Should be given after meals and tablets should be chewed

Thiabendazole has anti-inflammatory, analgesic and antipyretic actions. These may contribute to its effect cutaneous larva migrant and other inflammatory conditions produced by larvae or worms in tissues.

Thiabendazole inhibits dermatophytic fungi also.

Cont...

Pharmacokinetics: Thiabendazole is rapidly absorbed. It is metabolized to inactive metabolites and excreted in urine.

Adverse effects: These are frequent and often interfere with normal activity.

Nausea, vomiting, loss of appetite, headache, giddiness are most common.

Itching, abdominal pain, diarrhea and a variety of other symptoms are also produced

It should be avoided in pregnancy, liver and

1. Anticestodal drug

Niclosamide
(Mansonil®)



A salicylanide derivative Vermicide drug for treatment of tape worm infestation in dogs & cats, Beeftape worm, pork tape worm and fish tape worm. Has also activity against intestinal flukes as *paramphistomes* in ruminants

Not effective against cysticercosis or hydatid disease.

MOA: Adult worm killed by inhibiting the mitochondrial phosphorylation process thus inhibiting energy production in worms.

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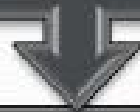
Pharmacokinetic: Niclosamide poorly absorbed & very rapidly excreted. Given in a single dose on

- It effective against cestodes infesting man – T.saginata , T.solium , D.latum , H.nana , thread worm .
- It safe during pregnancy

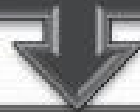
Hymenolepis
nana

Mech. Of action

Inhibit oxydative phosphorylation in mitochondria



Interfere with anaerobic generation of ATP by the tapeworm



Cause injury & partly digested in the intestine

2-

Bunamidine:

Used as Effective remedy for tape worms infesting dogs & cats.

MOA: act as vermicide by disruption of the tegument (outer skin) of worms and kill the worms.

Used for a long time as effective for *Echinococcus* in po

Adverse Effects: Diarrhea & vomition . sudden death dogs may happen as drug cause myocardial sensitization catecholamine.



3- Dichlorophen:

A narrow spectrum anthelmintic against *Taenia* & *Dipylidium* speices in dogs, but ineffective against *Echinococcus*.

31

MOA: as taenicide by inhibiting phosphorylation process in mitochondria

4-

Prazequentel



A broad Spectrum(Novel Anthelmintic)

Actives against Cestodes – Schistosomes -Trematodes

Effective against all adult **Cestodes** & their larval forms in dogs & cats

Active on **Trematodes** as the lung and gut flukes in animals, but not effective against liver flukes

MO A : Act as vermicide by 1- interfering with ionic balance due to leakage of IC Ca. from membrane causing paralysis.
2. Disruption of worm tegument & death.

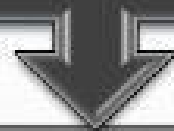
kinetics: Praziquantel given orally or (S/C) . Rapidly absorbed &

Metabolized its safety margin reaches 1:40 of the recommended

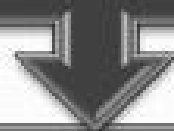
- ✓ Novel anthelmintic
- ✓ Active against Schistosomes, Trematodes & Cestodes

Mech. Of action

Acts by causing leakage of IC Ca from the membrane



Contracture & Paralysis



worm loses its grip in git & expelled out

5- Epsiprantel

A very potent, safe and novel tape worm reme

Given orally for treatment of cestodes of dog

Safer than praziquantel as its safety margin is

Not active against schistosomes.



MOA: anticestodal in a similar manner of praziquantel

6- Nitroscanate:

**Like dichlorophen, but more safer
(safety margin 1: 40)**

**A broad spectrum anthelmintic against cestodes &
nematodes of dogs but not used for cats.**

**MOA: Taenicide by inhibiting phosphorylation process in
mitochondria of worms so inhibit energy production.**

2. Antinematodal drug

1. Benzimidazoles



Benzimidazoles (**Albendazole**, **Thiabendazole**,
Triclabendazole ,

Mebendazole, **Oxfendazole** , **Fenbendazole** & **Flubendazole**).

A good activity against GIT nematodes & lung worms and their larvae.

The recent drugs **Mebendazole** & **Oxfendazole** are highly effective against both nematodes & cestodes(broad spectrum) .

Albendazole active against adult liver flukes, cestodes & GIT nematodes larvae (broad spectrum ,vermicide, oral anthelmintic)

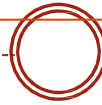
MOA: Benzimidazoles act as vermicide by inhibiting energy production via inhibition of the activity of fumarate reductase enz.

Benzim. are very safe anthelmintics ; a wide safety margin from 1: 20 for albendazole to 1: 100 for fenbendazole (very safe).

Albendazole leave tissue residues therefore 10 days from the last dosing of sheep and 14 days from the last dosing of cattle must be elapsed before slaughtering animals.

Cows producing milk for human should Not treated with Albendazole.

Clinical uses of Albendazole



Albendazole is the drug of choice for treatment of intestinal round worms as **Ascaris** , **hook worm** (Ankylostoma) **thread worm** (Strongyloids) , **pin worms** (Enterobius) & **whip worm** (Trichuris trichuria) infestations, as a single dose repeated after 3 weeks .

Albendazole is the main drug for **Hydatid disease** (dog tapeworm) twice / day & repeat after 2-3wks if required up to 3 courses.

(Morantel, Pyrantel & Oxantel)



Morantel effective against GIT nematodes, but not against lung worms in ruminants.

Used as a drench or "protectbolus" to provide prolonged protection for 90 days (slowly released).

Pyrantel pamoate:

A broad spectrum anthelmintic, highly effective against adult & larval nematodes of horse and dogs.

Not active against lung worms and whipworms.

Oxantel : Narrow spectrum (only active against whipworm) dogs

MOA: Pyrantel is a depolarizing neuromuscular blocking agent cause release of acetylcholine & inhibition of cholinesterase enz. leading to muscular paralysis & death (Vermicide)



Mech. Of Action

Activation of nicotinic cholinergic receptors in worm



Persistent Depolarization



Contracture & Spastic Paralysis of worm

Pyrantel Clinical

uses :



Pyrantel is very safe remedy for horses and dogs

Pyrantel Given to pregnant or lactating animals.

Pyrantel given orally with or without food.

For Pin worm, Ascariasis & Hookworm as a single dose and repeated after 2 wks.

Morantel is a very safe remedy and no withdrawal period is required for the bolus, but a withdrawal period of 3 days is required for the drench.

3- Levamisole & Tetramisole

Levamisole: Effective against mature and immature larval GI round worms. Used with limited success against heartworm microfilaria in dogs.

Very rapid action & expel worms within 24 hrs.

Rapid absorbed from GIT- Metabolized by liver-
Half life 3-4hr

Levamisole acts also as an immunostimulant drug if given to pregnant animals
MOA: N_N agonist stimulate nicotinic ganglia in causing muscular paralysis & death of the worms (vermicide).

Interfere with carbohydrate metabolism.



4-

Piperazine



Commonly used drug against worms in man and animals.

antinematodal only *Ascaris* and *Oxyuris*

Not recommended for other helminthes infestation.

Administered as citrate or phosphate salts and given orally as a

drench or added to drinking water for poultry.

MOA: act as vermifuge by its GABA agonist effect so it prevents neural transmission in the worm causing muscular paralysis and expelling of the worms

A very safe drug for man and animals during pregnancy



✓ It highly active drugs against ascaris , enterobius .

✓ It safe during Pregnancy .

Mech. Of action

Gaba agonistic action opening cl- channels



Hyperpolarization & Relaxation of ascaris muscle



Flaccid paralysis & Expels alive worms

5- Diethyl Carbamazine (DEC)



A highly soluble piperazine derivative → rapidly absorbed &

distributed throughout the body.

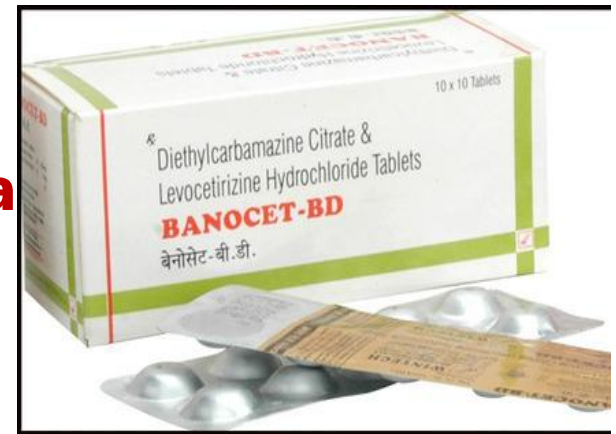
Drug of choice for treatment of **Filaria**

Highly selective effect on microfilaria.

Enhances cell mediated immunity

Used for control of heartworm larvae in dogs.

Safe for use in pregnant & young animals(Not teratogenic).



MOA: 1- DEC Immobilize microfilaria & alter their membrane structure displacing them from tissues & making them susceptible to destruction by host defense mechanism.

2.Alteration of microfilaria membrane → phagocytosed by fixed tissue monocytes.

3.Affect muscular activity and cause hyper polarization due to piperazine moiety.

The drug should be given after meals.

6- Ivermectin (Ivomec®)



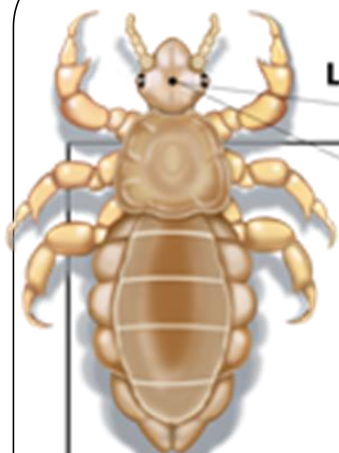
One of **Avermectins** that commonly used in vet. Med.

Highly effective against all nematodes in animals & arthropods as mange mites, lice & ticks (endectocide).

has no activity against cestodes and flukes.

Given S/C at very low doses (0.2mg /kg for cattle, horse & sheep)

MOA: act as **neurotransmitter** vermicide causing paralysis of worms by intensifying the action of the inhibitory transmitter GABA at neuromuscular junction → paralysis and death of the worms.



Louse

Normal nerve transmission

Sklice Lotion interrupts nerve transmission

Ivermectin binds selectively and with high affinity to glutamate-gated chloride channels leading to an increase in permeability of the cell membrane to chloride ions

Cell membrane

Chloride ion

Glutamate binds to receptor on channel and opens channel

Chloride ions pass through channels

Glutamate-gated chloride channels (enlarged) are found in cell membrane

Nerve impulse is generated and muscle is innervated

Ivermectin

The increased influx of chloride ions causes hyperpolarization of the nerve or muscle cell

Nerve impulses cannot be generated. This results in paralysis and death of the louse

Pharmacokinetic

S

Rapidly absorbed & widely distributed .

Does not cross BBB

Half- life 2-3 days & Excretion mainly in feces.

Very safe remedy for ruminants, with withdrawal period = 28 days

Not used in dairy cows providing milk for human consumption.

Contraindication:

Concurrent use with other drugs that enhance GABA
e.g Barbiturates, valproaic acid & benezodiazepines.

7- Organophosphate compounds



Organophosphates as diclorvos, haloxon, & trichlorphon.

Effective against GI nematodes infesting animals.

MOA: Organophosphates inhibit the acetylcholinestrerase of the

worms leading to their paralysis and death.

Nowadays, they are less commonly used because of their high toxicity to the host.

3. Antitrematodal drug

Benzimidazole derivatives:

1- Tricalbendazole.

2- Albendazole.

Tricalbendazole has **No** antinematodal activity but active against liver flukes (***Fasciola hepatica***) in sheep, goats and cattle

Triclabendazole very active against all stages (adult, immature larvae) of *Fasciola hepatica* from day 1 to adult worms.

Control & complete eradication of fascioliasis occur by breaking

L.C. liver flukes with triclabendazole once every 6-8 months .

A withdrawal time of 28 days for meat

Should not given to animals providing milk for human consumption

2- Albendazole:

widely used for combating round worms & liver flukes in ruminants.

Available as intraruminal bolus for sustained release of Albendaz.

Benzimidazole pro-drugs:



Netobimin is a pro-drug of albendazole.

When Netobimin dosed to sheep & cattle metabolized to Albendazole then converted to albendazole sulphoxide → excreted

Netobimin active against GI nematodes & their larvae, tape worms and flukes (broad spectrum anthelmintic).

Given orally or by injection.

A withdrawal period for meat = 5 days in sheep & 10 days in cattle.

A withdrawal period for Milk = 3 days in sheep & 2 days in cattle

Table 3: Clinical uses of Vet.Anthelmintics

Principal use	Drugs
Liver flukes in ruminants	Rafoxanide - Nitroxylnil- Clorsulon - Closantel- Albendazole- Oxcyclozanide - Triclabendazol
Round worms in ruminants	Phenothiazine- Morantel- Levamisole Albendazole - Ivermectin- Febantel
Round worms in horse	Ivermectin - Piperazine- Pyrantel- Dichlorvos Albendazole-Oxibendazole- Oxfendazole
Roundworms in dogs and cats	Nitroscanate- Dichlorvos Levamisole - Ivermectin- Piperazine
Tapeworms in dogs and cats	Niclosamide- Bunamidine- Dichlorophen Epsiprantel- Praziquantel

Anthelmintic combinations



Means finished formulated product has different anthelmintics to increase the spectrum of activity .

Drug mixtures are truly **complementary** ,e.g. ttt of round worms & flukes in ruminants and round worms & tape worms in dogs.

the drug mixtures interact with each other
e.g.combination of piperazine and phenothiazine (both antinematodal)

The most Common anthelmintic combinations :

1- For ruminants:

(a) Fasciolicide + antinematodal drug.

(b) Fasciolicide + trace element as cobalt or selenium.

2- For horses:

Drug combinations	Activities	Hosts
Ivermetin + Clorsulon	Round worm, adult fluke	Sheep , cattle
Thiabendazole + Rafoxanide	Round worm, adult fluke	Sheep , cattle
Levamisole + Oxyclozanide + Cobalt + Selenium	Round worm, adult fluke , trace element deficiency	
Rafoxanide + Oxibendazole + Cobalt	Round worm, adult fluke, cobalt Deficiency	
Morantel + Diethylcarbamazine	Round worm, lung worm	Sheep , cattle
Mebendazole + Trichlorphon	Round worm, bots	Horse
Thiabendazole + Piperazine	Round worm and ascarids	Horse
Pyrantel + Oxantel	Round worm & whip worm	Dog
Praziquantel + Febantel	Round worm, tape worm	Dog

ANTIPROTOZOAL DRUG

ANTICOCCIDIAL DRUGS.

The major drugs used are classified as

Sulphonamides

eg. Sulphadimidine with trimethoprim or
ormethoprim, sulphadiazine with
trimethoprim

Quinazolines

Quinolone

Symmetrical triazinones

Thiamine antagonists

Cont...

Quinazolines

Example halofuquinone

It is potent drug.

It can be used in avian species

Use:

Usually used in chicken

Dosage: chicken 3ppm in feed

Cont...

QUINOLONES.

Examples: Methylbezoquate

Quinolones: Their activity is essentially coccidiostatic used against invading sporozoites.

Should be used in early stage or prophylactically the drug would not be effective if delayed.

Mechanism of action.

The quinolones selectively inhibit the electron transport chain in the emeria parasite.

Use: For prevention of coccidiosis in chickens

Cont...

SYMMETRICAL TRIAZINONES

Example :- Toltrazuril

This is a drug produced for its coccidiostatic property used against sporozoites

It is also potent schizogony and gametogony

Spectrum of Activity

It is effective against *E. tenella*

It is used in turkeys, rabbits and chicken

Dosages

Broilers 25ppm in drinking water

Rabbit 10-15ppm

Cont...

THIAMINE ANTAGONIST

e.g Amprolium

Spectrum of Activity

It is used in confirmed *E. acervulina* and *E. tenella*

Some times used with sulpha drug to potential its activity

It is used in chickens, rabbits and ruminants.

Dosage

125- 150ppm in feed continuously

cont...

5mg/kg in water in calves for 21 days for treatment and used for 5 days for prophylaxis

Contraindication

The drug “Amprolium” should not be used for a long time without using vitamin supplement, because it might predispose the flock to thiamine deficiency.

ANTI TRYPANOSOMAL DRUGS

Diminazene aceturate, Phenamidine,
Stilbamidine and Pentamidine.

⌘ Diminazene aceturate -

It is odourless

Soluble in water

Slightly soluble in organic solvents.

Cont..

Indication

Trypanosomosis in early stage

Babesicidal effect or in babesia infection.

It has bactericidal effect against streptococcus.

Side Effects

Local reactions in horses and rats might occur at site of injection.

Neurotoxicity in dogs especially exotic breeds, ataxia, convulsion.

Nephrotoxicity may be induced by the drug.

Cont...

PHARMACOKINETICS

It is poorly absorbed orally

But the drug is rapidly absorbed intramuscularly and subcutaneously.

Distribution of the drug in the tissues is rapid and wide

The main drugs used for treatment of giardiasis are follows: Metronidazole, dimetridazole, pronidazole, tinidazole, nimorazole these are know as 5 - nitroimidazoles

Spectrum of Activity -It possesses a broad spectrum of activity.

It is effective against trichomonads, amoebae and giardia and bacteria (anaerobic cocci and bacilli).

Cont...

Pharmacokinetics- The oral bioavailability of metronidazole varies from 50-100%. If given with food absorption is enhanced in dogs.

Peak blood levels reaches in 1 hour of dosing.

Distribution is wide and rapid due to lipid solubility

Elimination half -life is 3-5 hours in dogs and horses.

Excretion takes place in 24 hour, the drugs

Metronidazole

Nausea, vomiting, abdominal cramp

High doses in dogs may produce neurological disturbances characterized by tremor, weakness, muscle spasm, ataxia and convulsion

Experiments in rats show that it is mutagenic if used for a prolonged time