College of Veterinary Medicine
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ANTIPARASITIC AGENTS
(ANTHELMINTIC DRUGS)

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Antiparasitics:-:-

drug that reduce parasite burdens to a tolerable level by killing parasites or inhibiting their growth.

Ideal anti parasitic: •

1. Has a wide therapeutic index (toxic dose > x time the therapeutic dose)
2. Effective after one dose.
3. Easy to administer (in feed,injected,pour-on).
4. In expensive.
5. No residue problem(in food-producing animals).
6. Effective agonist immature form of parasite.

General mechanism of action :•

1. Paralysis of parasites by mimicking the action of putative neurotransmitters.
2. Alteration of metabolic processes.
   a. Inhibition of microtubule synthesis .
   b.Inhibition of folic acid synthesis and metabolism.
   c. Inhibition of thiamine utilization.
   d.Uncoupling of oxidative phosphorylation

3. Alteration of parasite reproduction .
   a. Inhibition of replication in protozoans.
   b. inhibition of egg production in nematodes.

4. current trends include the use of broad-spectrum drugs and combination therapy to increase efficacy.

Antinematodal drug (Nematocides):-

1. Benzimidazoles (albenazole, fenbendazole, oxfendazole).
2. Nicotine agonists (Levamizole, pyrantel, morante).
3. Macrocyclic lactose (ivermectine).
4. Miscellaneous nematocides (dichlorovos , piprazine).

-Benzimidazoles (BZDS)(1

1-Thiabendazole:

Is aprototypical agent , use in rumenants & horses

No longer use because less potent than other BZDS

(Albendazole , Fenbendazole, Oxfendazole , Febantel)

Mechanism of action:- •

BZDS inhibit microtubules synthesis in nematodal cell by interfering with polymerization of β-tubuline.

Benzimidazole induced inhibition of microtubules synthesis in helminthes. BZDS binds β-tubulin of helminthes preventing dimerization with α-tubulin and polymerization of tubulin oligomers into microtubules.

Therapeutic uses:-

Ruminants:-Albendazole , fenbendazole and oxfendazole:-

1- against major GIT worms(adult, larval stages)

2- against lung worms

**** ineffective agents filariae.**

Horse :- fenbendazole, oxfendazole, oxibendazole

Against strongyles, oxyuris , trichostrongylus and parascaris

Dogs and cats :- fenbendazole and febantel

against ascaris , hookworms, whipworms (adult and larval forms)

** BZDS ovicidal activity on nematodes •

,** egg production inhibited within 1hour

given **orally** one single dose (**BZDS** • cattle , horse)

3-5 consecutive daily dose in carnivores • & omnivores.

* **Drug residues persist (1-3) weeks**

***Preslaughter period** :-

(27 dayes) in cattle:- albendazole ,**fenbendazole(**8days),oxfendazole(7days)

** Not uses in lactating dairy cattle (except fenbendazole)

** **Adverse effects** :- (the agents safe) .**

Albendazole:

(Teratogenic and embryotoxic) **

2)- Nicotinic agents :-

1-Levamizole:- orally , parenteral , topical or pour-on administration

Mechanism of action :-

paralyzes of worm by selectively activating

nematodal nicotinic receptors, entry Na, Ca, excessive body muscle contraction, then paralysis.

Uses

In ruminants :- against mature GI worm , long worm

Preslaughter clearance period :- In cattle :- 48-72h (p.o), 7 days (s.c) , 11 days (topical).

Adverse effects:- is most toxic anthelmintic , low safety margin especially injection .

** Don't administer to dairy cattle.

In horse:- of poisoning sings are depolarizing blockade of skeletal muscle (no antidote).

**Coadministration of levamisole and pyrantel lead to nicotine- like nematocide (increases toxicity) .

2- Pyrantel and morantel:-

Mechanism of action :- paralyze worm by causing depolarizing neuromuscular blockade (like levamisole)

Uses:-

Horses:- strongyles, ascaris, pinworms.

Dogs& cats:- pyrantel effective agenist GITnematodes.

Ruminnants:-Morantel against stomach worm, nodular worm.

Adverse effects:- Similar to levamisole

Contraindication:- note use concurrently with levamisole.

3)-Macrocyclic lactone:-

Antibiotics derived from Streptomyces, activating against nematodes& arthropods (dose in µg/Kg) .

Example:- **Ivermectine**

Mechanism of action :- activated glutamate-gated chloride lead to

inhibiting neurotransmission lead to increase Cl conductance in nematode lead to flaccid paralysis

***Adverse effects**:- highly safety margin in ruminants , horse, safe for pregnant animals.

Collies dog , Murray cattle are high sensitive to ivermectine.

* local irritation following S.c. injection

Uses:-

Cattle :- effective against GI worm and lung worm dose (0.2 mg/ kg orally , S.C.or 0.5 mg/ kg topically) * pour-on ivermectine as nematocide in cattle

Horse:- against bots , stomach worm , strongyles, pinworm, ascaris(0.2mg/kg orally), also against ectoparasit.

**Ivermectine :- against microfilaricide (50μ/kg, orally).

4)- Miscellaneous antinematodal drugs:-

1- dichlorovos :- organophosphate

** preslaughter period :- sheep 11 day(P.O) cattle 35 days (S.C), 49 days(P.0) .

****Should not be administered to dairy cattle > 20 month old**

Mechnisme of action**:- irreversible inhibition of acetylcholine esteras ⟶ increase in acetylcholine level**

2-Piperazine:-

Mechanism of action :-

is GABAA –receptor agonist hyperpolarizes nematode muscle flaccid paralysis of worm.

.Clinical uses :-

against ascaris & nodular worm , its use limited in ruminants because Ascaris not significant problem in this species.

Drug for heart worm prevention and therapy:-

Treat & prevention of heart worm involve 3 aspects:-

1. Treatment to elimination microfilaria.
2. Removal adult worm (requires an adulticidal).
   Intiated 3-4 week after adulticide treatment .

***Not:- microfilaricidal treatment ↓ the incidence of glomerulonephritis, which may be induced when microfilaria present in large number.

** microfilaria treatment elimination the source of heart worm infestation.

3- Prevention of infection (required a larvicidal).

**Adulticides elimition both immature & adult

↓

1. **Melarsomine** (immiticides)℞

Atrivalent arsenic compound , dose (2.5 mg/ kg) once aday for 2 days.

Note:- drug highly irritable ⟶ first injected into

1)- right lumber muscle, second into left.

2)- the 2 doses ⟶ eliminate all adult worm in 60-80 of treated dogs.

3)- repeated in 4 month ⟶ increase efficacy to 98%.

Mechanism of action :-

denatures protein / enzymes by binding to sulfhydryl group of cysteine residues.

***Microfilaricides**:-

2- Macrocyclic lactones(**Ivermectine)**:-

One dose (50µg/ kg) orally or S.C. ** **not use in collies**

*** **Larvicides for heat worm worm prevention** (ivermectine , moxidectin milbemycin) kill L_4 larvae

*** ivermectine give orally (6-12 µg/ Kg) once amonth.

Anticestodal drugs:-

These agents kill tape worm called(taeniacides)

1)- **Dichlorophene:-** treated taenia & Dipylidium in dogs and cats.

Given orally after overnight fast

Mechanism of action :-

uncoupling of oxidative phosphorylation deplete ATP for the tap worm &disrupts the PH difference across the external tegmental membranes.

2)- **Benzimidazoles:-**

fenbendazole, oxfenbedazole, albendazole all against adult *Echinococcus* in dogs and cats and moniezia in ruminants.

3)- **Praziquantel (Drocil) , rontal, Equimax :**

Effective against all species of tape worms

Mechanism of action:- causes paralysis and digestion of tape worms.

4)- **Epsiprantel:-** praziquantel analog**.**

5)- Pyrantel pamoate :- against equine tape worm

dose (13.2 mg / kg) orally.

Antitrematodal drugs:-

Infection with **liverfluks** (fasciola hepatica) in domestic animals.

1. Clorsulon (curatrem, ivomec plus).

Is sulfonamide effective against both mature and immature *F.heptica* in cattle .

Mechanism of action :-

Inhibit 3 phosphoglycerate kinase and phosphoglyceromutase in the glycolytic pathway ⟶ depriving the flukes of ametabolic energy source.

** safe in pregnant and breeding animals

2- Albendazole :- aganist mature liver fluckes **(*F.hepatica)*** in cattle.

Not:-1- withdrawal period preslaughter 27 days.

2-teratogenic , not use in pregnant cattle during first 45 days of gestation

3-praziquantel :-against lung flucks in dogs.Also effective against liver fluckes.

****Note**:- too expensive to use in ruminants

*__Anthelmintic resistance in large animals:-__

Definition :- when agreater frequency of individuals in a parasite population no longer respons to the clinical dose.

Management factors that affect the development of resistance

1-avoide under-dosing.

2-removal of feces and alterate grazing of different hosts .

3-use short –acting drug to prevent worm exposed to subtherapeutic concen .

4-use alterative anthelmintics with different mechanismof action.

5-inherent nature of the chemical (some anthelminitics allow resistance faster that other) fenbendazole is faster than ivermectine.

Antiprotozoal drugs:-

Anticoccidial druds , drugs for treatment of equine Protozoal myeloencephalitis (EPM) toxoplasmosis , Giardiasis, babesiosis, cryptosporidiosis.

A)- **Anticoccidial drugs:-**

1-poultry:- **sulfonamides,and ormetroprim,diclozuril → To treat infected animals

*clopidol,decoquinte,zoalene,amprolium → to prevent coccidiosis.

Anticoccidial agent:

1-Decoquinate:-

In cattle, sheep ,goat and broiler to prevent coccidiosis

Not Effective to treat clinical coccidiosis

(use as food additive).

Mechanism of action:-

inhibiting electron transport with Parasite mitochondria

(may block DNA synthesis).

2-Clopidol:- food additive to prevent coccidiosis in chickens.

3-Na^+ ionophors:- (monensin, lasalocid, narasin,---)

Antibiotics used exclusively as anticoccidal drug in chicken.

Monensin:-

In cattle , goat ,broiler

Mechanism of action :-

Facilitate the transport Na^+ and H^+ into cells in the rumen, elevating intracellular $Na^+$and H^+into cells in the rumen , elevating intracellular Na^+ &H^+ concentration mitochondrial function & ATP hydrolysis are inhibited.

4-Amprolium:-

only anticoccidial agent used in laying birds & cattle for both prevention & treatment of outbreaks.

Mechanism of action:-

Prevent coccidian from utilizing thamine by blocking thamine receptors.

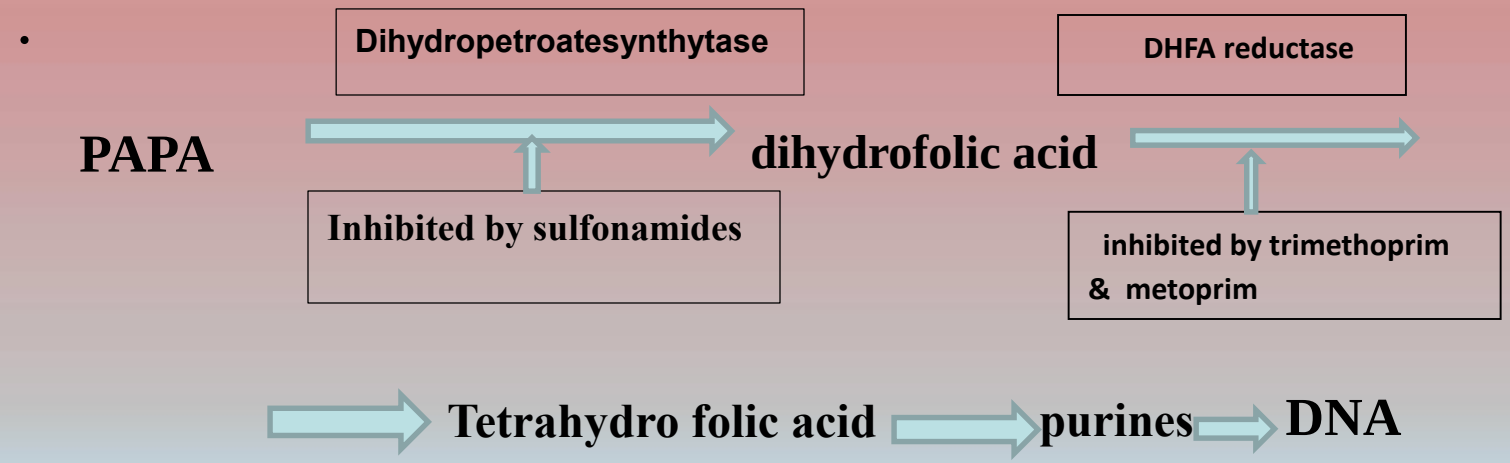
Side effects:-Neurological signs & lesions of thamine deficiency in host following extremely high overdose

5-Sulfonamides:-

(sulfadimethoxine, sulfamethazine, sulfaquinoxaline).are abroad spectrum (protozoa& bacteriostatic)

Mechanisme of action

competitively inhibit (dihydropteroate synthase , the enzyme which catalyzes the incorporation PABAinto dihydrofolic acid



*****Folic acid is required for purine & DNA synthesis , thus bacteria growth is inhibit.

*** ammamlian cells & bacteria that use preformed folic acid are not affected

Therapeutic uses:-

prevention and treatment of local and systemic infection in all specie

6-Dihydrofolate reductase inhibitors:- (pyrimmethamine not approved for food animals).

7- Toltrazuril and ponazuril:-

effective against schizents and gamets by inhibiting nuclear division

B)- Metronidazole (flagyl):-

Mechanism of action:-

aferrodoxin- liked metabolite of metronidazole disrupts DNA synthesis in protozoans and bacteria.

Uses :-

broad spectrum antiprotozoal drug. Against giardia,Histomonas, babesia, trichomonas, (ameba).

Side effects:

because affected DNA synthesis teratogenic & carcinogenic effects

Treatment of giardiasis:-

Albendazole, fenbendazole (orally at 25 mg/ kg) every 12h for 2 days.

****Drugs for treatment of toxoplasmosis:-

1. Trimethoprime – sulfaiazine (15 mg/ kg p.o. twice aday for 4 weeks).
2. Clindamycin:- (10-20 mg/kg P.O. orI.M. twice aday for 3-weeks).**

Drugs for treatment of cryptosporidiosis:-

1-Paromomycin (Humatin).:-

is aminoglycosides , very expensive (prevent & treat at 50mg/kg p.o. 2 daily for 10 days).

2- Azithromycin (Zithromax) .

(15 mg/kg P.O.twice aday for treatment crypto.

Drugs for treatment of Babesiosis:-

Imidocarb (imizol)

Mechanism of action :-

binds to DNAand inter with parasite replication

Therapeutic uses:-

* against babesia cains (dogs) .*bovine babesosis not .

.* not be give to bovine because with drawal period not been determind.

*feline babesosis.

Side effects:-

1. Pain During injection.
2. Sings of stimulation (salivation) nasal drip, restlessness, vomiting, which lasting one- several days.
3. Teratogenic & carcinogenic .

Not use in pregnant animals

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External antiparasitic (Ectoparasiticides):-

Insecticides are used to:-

1. Control mites , fleas , ticks and flies.
2. On the premise to control flies and other insects.
3. On feed stuffs.

***Formulation :-

a. Sprays, dips & shampoo.

b. Pour- on and dust.

c. Oil sprays (on hair coat to the skin to avoid systemic absorbed).

d. Feed additives (absorbed and affected against blood suckling parasites.

e. Collars and ear tags.

a.Organophosphates(Ops) :-

* insecticides (couaphos , fenthion, diazinon, ethion, famphus).

*Oxy compounds (dichlrovos, tetrachlorvinphos).

Mechanism of action :-

The OP insecticides inhibit Ach breakdown by inhibition chE irreversibly

Note:-

The thiocompounds are week chE inhibitors , must be metabolized to oxy compounds to inhibit chE

B-Carbamates:-

*carbaryl

*propoxur

Treat ectoparasites in small animals& powder, shampoo&collar formulation.

Mechanism of action:-

inhibit chE via carbamylation reversible (bindind between carbamate & chE is non covalent).

Adverse effects:-

toxicity similar to Ops

Treatment :-

Atropine sulfate.

******2-PAM should **Not** be used to treat carbamates

Poisoning for two reasons:-

1- carbamat binding to chE reversible.

2- 2PAM it self inhibit chE in irreversible manner.

C- Chlorinated hydrocarbons:-

1. DDT , methoxychlo

Mechanism of action :- increase intracellular $(Na)^{+}$and$(Ca)^{+}$of excitable cell via

a. High Na lead to depolarization

b. Ca overstimulation neurotransmission paralyze the insect.

Uses:- Methoxychlor (powder& sprays) to killfleas, ticks, flies, mosquitoes.

Side effect of DDT:-

Has environmental hazara:- because DDTmetabolised to DDD & DDE.

DDE is lipid soluble & cant metabolized store in → adipose tissue of animals ⟶ residue problems

⟶

2-Lindine:-

Mechanism of action :-

blocking GABA-gated chloride channles → Excitability

.

Side effect:- **Lindine** more toxic than DDT.

D- Botanicals:-

1-Rotenone:- inhibit cellular respiratory metabolism by blocking the electron generation from reduced nicotinamide adenine dinucleotide(NADH). → Never conduction is inhibit

Uses:- kill fleas , lice, mites

2-Pyrethroides:-

Pyrethrins, allerthrin, cypermethrin, permethrin)

Mechanism of action:-

Increase excitability of ectoparasite neurons by prolonging the opening of Na^+channles → arthropod paralysis.

***Other ectoparasiticides:-

- A mitraz → flaccid paralysis
- Insect nicotinic receptor agonists (as imidocloprid) which activated nicotinic receptors of fleas lead to overstimulation of neuron & muscle then cause paralysis.

Thank you