

# ANTHELMINTICS



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# ANTHELMINTICS

**Definition:** These are drugs which kill or expel the internal parasitic worms living in GIT and other tissues of man and animals.

## **Characteristics of ideal anthelmintic:**

- 1- Broad (WIDE) spectrum of activity. i.e. Act on different types of worms.**
- 2- Wide therapeutic index (safe). i.e. At least 1:6, highly toxic to the worm and less toxic to the host.**
- 3- No or few tissue residues. i.e. short residence time.**
- 4- Easily administered.**
- 5- Economic not expensive.**

# Classification of anthelmintics

## (I) According to the type of action:

**1- Vermifuge:** Expel the worm alive. e.g. Santonine-  
Arecoline- Piperazine.

**2- Vermicide:** Kill the worm. e.g. Bunamidine-  
Praziquantel- Phenothiazine.

## (I I) According to the spectrum of activity.

**1- Narrow spectrum:** e.g. Nitroxylnil: Active only against  
adult liver flukes.

**2- Broad spectrum:** e.g. Benzimidazoles: Active against a  
wide range of GI nematodes and some are active  
against liver flukes.

**3- Endectocides:** These are drugs effective against both  
arthropods and nematodes.

e.g. Avermectins AND Milbemycins.

# **Classification of anthelmintics**

## **(III) According to the type of worm:**

**1- Anticestodals → Tape worms.**

**2- Antinematodals → Round worms.**

**3- Antitrematodals → Flukes.**

# General Mechanisms of action

## 1- Drugs inhibiting energy production by:

**A-**Inhibiting activity of fumarate reductase enzyme in the parasite: e.g. Benzimidazoles (BZM).

**B-** Inhibiting mitochondrial phosphorylation process in the parasite:  
e.g. Niclosamide- Rafoxanide- Dichlorophen.

**C-** Inhibiting process of glycolysis: e.g.  
Phenothiazine- Clorsulon.

# General Mechanisms of action

## 2- Drugs causing muscular paralysis of the worms by:

**A-** Inhibiting cholinergic nerves of the parasite. e.g. Nicotine sulphate.

**B-** Acting as GABA agonist so paralyze the worms.e.g. Ivermectin- Piperazine.

**C-** Causing muscle hyperpolarization. e.g. Levamisole- Pyrantel.

## 3- Other mechanisms:

By causing disruption of the tegument of the parasite.e.g. Bunamidine- Praziquantel.

# ANTICESTODAL DRUGS

## Definition:

These are drugs which kill or expel cestodes (tape worms) infesting man or animals.

## Classification:

### (A) Organic drugs of plant origin:

#### 1- Arecoline:

It is an alkaloid obtained from areca nut seeds.

Action: Vermifuge.

Act on: Cestodes especially Taenia of dog and cat.

M.O.A: It causing muscular paralysis of worms so they loose their attachment with intestinal mucosa of the host. Moreover, it increase their intestinal motility of the host (due to the muscarinic action) (neuromuscular purgative) so it expel the detached worms.

# ANTICESTODAL DRUGS

(A) Organic drugs of plant origin:

## 2- Kamala:

It is red powder of Kamala tree.

**Action: Vermifuge.**

**Act on: Cestodes of poultry.**

**M.O.A: It acts by irritating muscle of the worm, increasing its motility, so loose its fixation with intestinal mucosa.**

# ANTICESTODAL DRUGS

## (B) Synthetic drugs:

### 1- Bunamidine:

**Action: Vermicide.**

**Act on: Cestodes especially Echinococcs of dog and cat.**

**M.O.A: By causing disruption of the tegument (outer skin) of the parasite.**

**Side effects: Diarrhea and vomition. Sudden death in dogs was due to drug effect on the heart causing myocardial sensitization to catecholamines.**

# ANTICESTODAL DRUGS

## 2- Niclosamide ( Mansonil):

Action: Vermicide.

Act on: Cestodes of dog and cat and intestinal flukes ( paramphistom) in ruminants.

M.O.A: Inhibiting mitochondrial phosphorylation process in the parasite so inhibiting energy production.

## 3- Praziquantel:

Action: Vermicide.

Act on: Cestodes and their larvae- lung and intestinal flukes- Schistosom.

M.O.A: 1- It acts on the worm by interfering with the ionic balance of the muscle cells causing rapid muscular contraction.

2- It causing disruption of the tegument (outer skin) of the parasite.

## 4- Epsiprantel:

Act as an Anticestodals in a similar manner of Praziquantel, More safe (its safety margin is 1:90).

# ANTICESTODAL DRUGS

## 5- Dichlorophen:

It is a substituted phenolic compound.

Action: Taenicide.

Act on: Cestodes especially Taenia and Dipylidium.

M.O.A: Inhibiting mitochondrial phosphorylation process in the parasite so inhibiting energy production.

## 6- Nitroscanate:

It is a substituted phenolic compound.

Act as an Anticestodals in a similar manner of Dichlorophen. Act also on round worms.

Side effects: Vomition.

# II- ANTINEMATODAL DRUGS

## Definition:

These are drugs which kill or expel nematodes (round worms) infesting man or animals

## Classification:

### (A) Organic drugs of plant origin:

#### 1- Nicotine sulphate:

It is an alkaloid obtained from Nicotiana tobacco plant.

Action: Vermifuge.

Act on: Nematodes especially Ascaris and Trichostrongylus.

M.O.A: it acts by inhibiting cholinergic nerves so causing muscular paralysis and elimination of worms.

# II- ANTINEMATODAL DRUGS

## (A) Organic drugs of plant origin:

### 2- Santonine:

**Action:** Vermifuge.

**Act on:** Nematodes especially *Ascaris*.

**M.O.A:** it irritates the muscle of the worm, so increase its motility and loose its fixation with the intestinal mucosa.

### 3- Chenopodium oil:

It is volatile oil contain Ascaridol as active substance.

**Action:** Vermifuge.

**Act on:** Nematodes especially *Ascaris* and *Strongylus*.

**M.O.A:** by causing muscular paralysis of the worm and help their expulsion.

# II- ANTINEMATODAL DRUGS

## (B) Synthetic drugs:

### 1- Phenothiazine:

It is green powder, insoluble in water and given as an oral suspension.

**Action:** Vermicide.

Act on: GI nematodes and *Heterakis Gallinae* of poultry.

**M.O.A:** after absorption through the cuticle of the worm it inhibits the process of glycolysis, so inhibit energy production.

### **Disadvantages:**

a- Large therapeutic dose.

b- Moderate anthelmintic activity.

c- Its oxidative metabolite stains urine, feces and milk with red color.

Phenothiazine → phenothiazine sulphoxide → leucothional (red dye).

d- Its sulphoxide metabolites cause photosensitization in calves and keratitis and blindness in poultry.

# II- ANTINEMATODAL DRUGS

## (B) Synthetic drugs:

### 2- Piperazine:

Piperazine used in the form of citrate, phosphate, hydrate salts.

**Action:** Vermifuge.

**Act on:** Nematodes especially *Ascaris* and *Oxyuris*.

**M.O.A:** Acting as GABA agonist, prevent neural transmission inside the worm so paralyze the worms.

### 3- Diethylcarbamazine

is a highly soluble Piperazine derivative.

**M.O.A:** it disrupts microtubules and inhibits microtubule polymerization.

# II- ANTINEMATODAL DRUGS

## (B) Synthetic drugs:

### 4- Levamisole:

It is an imidazothiazole derivative, and wide spectrum anthelmintics.

**Action:** Vermicide and immunostimulant agent.

Act on: GI nematodes and lung worms.

**M.O.A:** causing hyperpolarization leading to muscular paralysis and death of the worms.

Toxicity: Excessive sweating and rapid respiration.

# II- ANTINEMATODAL DRUGS

## (B) Synthetic drugs:

### 5- Benzimidazoles (BZM):

This group includes thiabendazole, oxbendazole, parbendazole, cambendazole, fenbendazole, mebendazole, albendazole and triclabendazole.

They are wide spectrum anthelmintics.

**Action:** Vermicide.

**Act on:** GI nematodes.

**M.O.A:** inhibit energy production in the worm by inhibiting the activity of fumarate reductase enzyme.

**N.B.** Care should be taken during dosing pregnant animals because they have shown to produce embryotoxicity and teratogenicity.

# II- ANTINEMATODAL DRUGS

## (B) Synthetic drugs:

### 6- Tetrahydropyrimidines:

They include three commonly used drugs: Morantel, Pyrantel and Oxantel.

They are wide spectrum anthelmintics.

**Action:** Vermicide.

**Act on:** GI nematodes.

**M.O.A:** they affect the worm neuromuscular system causing hyperpolarization leading to muscular paralysis and death.

# II- ANTINEMATODAL DRUGS

## 7- Ivermectins:

It is effective against all stages of major nematodes in animals and also is potent ectoparasiticide against mange and lice. S/C injection.

It has no activity against tape worm and liver flukes.

**Action:** Vermicide.

Act on: Endoparasites (GI nematodes) and Ectoparasites (mange and lice).

**M.O.A:** it paralyzes the worm by augmenting the action of the inhibitory transmitter GABA, at the worm neuromuscular junction causing paralysis and death.

Withdrawal period: 28 days.

N.B: not used in dairy cows producing milk for human consumption.

# II- ANTINEMATODAL DRUGS

## (B) Synthetic drugs:

### 8- Organophosphorus compounds (OPC):

OPC such as dichlorvos, haloxon and trichlorphon (metriphosphate).

**Action:** Vermicide.

Act on: GI nematodes and Insects.

**M.O.A:** acts by inhibiting cholinesterase enzyme of the worm.

Toxicity: SLUDE.

# III- ANTI TREMATODAL DRUGS (ANTIFLUKES)

## Definition:

These are drugs which kill liver flukes (*Fasciola hepatica* and *gigantica*), duodenal, rumen and abomasal flukes (*paramphoestomes*) and blood flukes (*Schistosomes*) infesting man or animals.

## **(A) Old Fasciolicides:**

### **1- Carbontetrachloride (CCL<sub>4</sub>):**

It is given either orally as drench and capsules or I/M.

**Action:** Fasciolicides.

**Act on:** Mature worms but not affect immature flukes, so its administration is repeated after 3-4 weeks.

**M.O.A:** IT acts on mature worm only so it affects metabolic enzymes which found in mature worms and not found in immature flukes.

**Toxicity:** it may cause liver damage which may end with liver failure.

**Symptoms:** Hypocalcaemia, drowsiness, muscular incoordination or convulsion, diarrhea.

**Treatment:** calcium borogluconate I/V.

Inhibit protein intake

## **(A) Old Fasciolicides:**

### **2- Hexachloroethane (C<sub>2</sub>Cl<sub>6</sub>):**

Similar in action and M.O.A to CCL<sub>4</sub>.

Given orally in the form of aqueous suspension or bolus.

Less toxic to the host than CCL<sub>4</sub>.

Toxicity: loss of appetite and diarrhea.

## **(B) Modern Fasciolicides:**

### **A- Substituted phenol:**

#### **1- Nitroxylnil:**

It is one of substituted phenols.

It is only active by S/C injection, because if it is given orally reduction of nitro group by ruminal MO causes loss of its anthelmintic activity.

**Action:** Vermicide.

**Act on:** It is active against adult liver flukes and has some activity against fly larvae.

**Withdrawal period:** 30 days.

N.B: not used in dairy cows producing milk for human consumption.

## **(B) Modern Fasciolicides:**

### **A- Substituted phenol:**

#### **2- Diamphenethide:**

**It is one of substituted phenols.**

**Action:** Vermicide.

**Act on:** It is highly effective against mature and immature flukes in sheep, but not in cattle.

**M.O.A:** It cause rupture of the fluke tegument and induce paralysis.

**Withdrawal period:** 7 days.

**N.B:** not used in sheep producing milk for human consumption.

## **(B) Modern Fasciolicides:**

### **B- Salicylanilide derivatives:**

#### **1- Rafoxanide:**

It is a salicylanilide derivative.

**Action:** Vermicide.

Act on: It is highly effective against mature and immature flukes in sheep and cattle; it is also active against blood suckling nematodes.

**M.O.A:** Inhibiting mitochondrial phosphorylation process in the parasite so inhibiting energy production.

Withdrawal period: 28 days.

N.B: not used in dairy cows producing milk for human consumption.

## **(B) Modern Fasciolicides:**

### **B- Salicylanilide derivatives:**

#### **2- Closantel:**

It is a recent analogue of salicylanilides.

**Action:** Vermicide.

**Act on:** It is highly effective against mature and immature flukes in sheep and cattle; it is also active against blood suckling nematodes. As well as some external parasite as mange mites and ticks.

#### **3- Oxyclozanide:**

It is a salicylanilide derivative. Act as an oral fasciolicide.

**Action:** Vermicide.

**Act on:** It is effective against adult liver flukes.

**Withdrawal period:** 14 days for meat, but for milk is zero because not excreted in milk.

## **C- Sulphonamide derivatives:**

### **Clorsulon:**

It is a sulphonamide derivative.

**Action:** Vermicide.

**Act on:** It is effective against mature and immature flukes.

**M.O.A:** Inhibiting the process of glycolysis, so inhibit energy production.

**Withdrawal period:** 8 days for meat and may be not used for lactating cows.

## **D- Benzimidazole derivatives:**

### **1- Triclabendazole:**

It is one of recent BZM.

**Action:** Vermicide.

**Act on:** It is active against all parasitic stages of *Fasciola* in both sheep and cattle.

It has no activity against nematodes.

**M.O.A:** like other BZM.

### **2- Albendazole:**

It is widely used for combating round worms and liver flukes in ruminants.

It is active against all important nematodes and their larvae including hypobiotic larvae. It is also active against tape worms and adult liver flukes.

**Withdrawal period:**

Sheep: 10 days

Cattle: 14 days

**M.O.A:** like other BZM.

## **E- Benzimidazole pro-drugs:**

### **•Netobimin:**

*Netobimin* → *albendazole* → *albendazole sulphoxide and albendazole sulphone.*

**It is active against GI nematodes and their larvae, tape worms and adult liver flukes.**

### **Withdrawal period:**

**Sheep meat: 5 days  
days**

**Sheep milk: 3**

**Cattle meat: 10 days**

**Cattle milk: 2 days**

**M.O.A: like other BZM.**

# **Anthelmintic resistance: (Drug fastness):**

It means resistance of the parasitic worms to anthelmintic treatment.

## **Factors which predispose to the development of this phenomenon:**

**A** - The regular using of anthelmintic drug below its recommended dose.

**B** - The continued dependence upon single type of anthelmintic.

**C** - Excessive and indiscriminate treatment of animals with anthelmintics.

# **Anthelmintic resistance: (Drug fastness):**

**To avoid the occurrence of this phenomenon:**

**A** - Minimizing the frequency of dosing the anthelmintic.

**B** - Increasing the recommended dose of a resistant drug will cause cure until the worm become resistant to that dose too.

**C** - Alternative treatment between different anthelmintic drugs.

**D** - Combined treatment with a narrow spectrum anthelmintic.

# Anthelmintic combination

It is mean combination of different anthelmintics to increase the spectrum of activity of the finished formulated product.

The most common combinations:

## 1- For ruminants:

**A** - Fasciolicide + antinematodal drug.

**B** - Fasciolicide + trace element as cobalt or selenium.

**C** - Antinematodal + clostridia vaccine.

## 2- For horses:

Antinematodal drug is mixed with pesticide or anticestodal drugs.