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Anticoccidial Drugs Used in Poultry

Ionophores

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Ionophores

Description

- Ionophores are the fermentation products of *Streptomyces* and other fungi species, extensively used as anticoccidials.
- Commercial ionophores are;
  1. Monensin
  2. Lasalocid
  3. Salinomycin

Cont. ...

› Monensin is choice of product for broiler chickens mainly because of its broad spectrum activity against majority of pathogenic species of coccidian and lack of development of drug resistance.

Mechanism of Action

- Ionophores facilitate transport of Na ion in cells and elevates the intracellular concentration of Na ion.
- This increased concentration of Na ion inhibits the certain mitochondrial functions such as substrate oxidation and ATP hydrolysis.
- Intracellular Na ion exchanges for extracellular Ca and increases intracellular concentration of calcium ions lead to cytotoxicity.
- In addition some drugs directly facilitates Ca transport in cells and increased intracellular concentration of Ca in cardiac and skeletal muscle cells are responsible for its toxic effects in cells.

Monensin

Description

- It is a fermentation product of *Streptomyces cinnamonensis*
- It is the first antibiotic used as an anticoccidials.

Spectrum

- It acts on trophozoites and 1st generation schizonts.
- Its activity is generally within **the first 2 days** of life cycle of coccidian.

Cont. ...

Dosage

- It gives protection against all species at 0.01-0.121% concentration in the feed.
- It also increases the weight gain and feed conversion and in some cases causes suppression of necrotic enteritis.
- It is superior over amprolium, clopidol and zoalene in control of coccidiosis.
- In the USA, there is 3 days pre marketing withdrawal requirement for this compound.

Lasalocid

Description

› It is another fermentation product and has a high degree of anticoccidials activity.

Dosage

› It is effective at 0.005-0.0075% concentration.

› It also increases weight gain, feed conversion and reduces the lesion in severe coccidiosis.

Salinomycin

Description

- It was isolated from a culture of *Streptomyces albus.*
- It is more closely related to monensin than lasalocid.

Dosage

- It has anticoccidials activity at 0.01 % in the feed and it was as effective as 0.0121% monensin in controlling coccidiosis.

Maduramicin

- **Description**
  - It is most potent among the polyether Ionophores.
- **Dosage**
  - It is given at 5-6 ppm in feed and activity is similar to that of other Ionophores.

Amprolium

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Amprolium

Description

› It is quarternized derivative of pyrimidine which is a thiamine antagonist.

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.

Cont. ...

Spectrum

- 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 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.

Cont. ...

Safety

- 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.
- 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.
- There is no premarketing withdrawal requirement for this compound.

Cont. ...

Dosage

- 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.
- 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.

Cont. ...

Resistance

- It is rarely used alone because E. *maxima* and other species are resistant and therefore given in combination with other drugs.
- Continuous use of Amprolium is resulting into the development of drug resistance which is a major problem and limiting its use.

Nicarbazin

Nicarbazin

Description

- It is an equimolecular complex of p, p'-dinitrocarbanilide (DNC) and 2-hydroxy-4, 6-dimethylpyrimidine (HDP).
- DNC is absorbed more rapidly from the chicken digestive tract but disappear more slowly from the tissues than HDP.
- Both are necessary for anticoccidial activity.
- This compound is used principally as a prophylactic and therapeutic dose lies near the toxic dose.

Cont. ...

Mechanism of action

- It is coccidiocidal.
- It can enter the cells of the coccidia and paralyze the intracellular energy-supplying ATP which leads to the interruption of cellular energy supply and the cease of function of sodium-potassium ion pump which results in the abundant influx of sodium ions and with them the influx of abundant water which causes the intracellular imbalance of ions in the cells of the coccidia or the rupture of the cells and the death of coccidia occurs.

Cont. ...

Spectrum

- Nicarbazine has a broad spectrum activity and effective against all *Eimeria* spp.
- This compound has coccidiocidal activity, mainly against the 2nd generation schizonts and moderate action on the sexual stages.

Dosage

- 0.0125% in feed
- It is available as a 22.5% premix
- Some strains of coccidia which have become resistant to other drugs remain sensitive to nicarbazin.
- The drug is suitable for administration to broiler flocks and it is usually given for the first 12 weeks of the chicken's life.

Cont. ...

Limitations

- It reduces egg production and hactchability.
- It causes depigmentation of eggs, mottled egg yolk and poor hatchability, so it should not be used for laying hens.
- Losses from heat stress may occur in broilers if they are medicated with nicarbazin.
- Withdrawal period in broilers: 4 days

Sulphonamides

Sulphonamides

- They have longest history of use as anticoccidial drugs.
- The common drugs of this group which are used as anticoccidials are:
  1. Sulphadimidine
  2. Sulphaquinoxaline
  3. Sulphadimethoxine
  4. Sulphanitran
  5. Sulphaguanidine

Cont. ...

Spectrum

- Sulphonamides have broad spectrum of activity against Eimeria 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 2nd generation schizonts of E. *tenella* and E. *necatrix*.
- They can act upon 1st 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

- Wood and Fildes proposed mechanism of action of sulphonamides as follows;
  - Coccidian is synthesizing their own folic acid utilizing PABA (p-amino-benzoic acid) from growing medium because folic acid is required for growth and 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.
  - Therefore they prevent proper development of schizonts.

Notes

- Animal cells also require folic acid but they utilize performed folic acid supplied in diet and are unaffected by sulfonamides.
- Diaminopyrimidines inhibits the conversion of folic acid to tetrahydrofolic acid and are used in combination with Sulphonamides to potentiate their anti coccidial action.

Sulphadimidine

Description

- This compound is still used as a curative drug in certain parts of the world.
- Its use has largely been discontinued in Western Europe and North America where it has been replaced by other compounds.

Spectrum

- It is active against E. *tenella*, E. *necatrix* and other species of coccidia.
- It has been used in the control of clinical outbreaks of coccidiosis.
- The problem of this drug is that it interferes with vitamin K synthesis in the intestine and resulting into prolongation of blood coagulation time.
- At higher doses it causes loss of egg production in laying hens and hyperplasia of the somniferous tubules of testicles of male birds.

Cont. ...

Dosage:

- 0.4% in feed
- 0.2% solution of the sodium salt in drinking water.

Sulphaquinoxaline

Description:

› It is an important, effective and commonly used coccidiostat throughout the world.

Spectrum:

› It is active against E. *acervulina* in addition to E. *necatrix* and E. *tenella*.

› It exerts marked inhibitory effects on schizogony.

Cont. ...

Dosage:

- For therapeutic purposes
  - 0.5% in the feed.
  - 0.043% In drinking water for 2 durations each for 2 days with 3-5 days intervals.
- Prophylactic purpose:
  - 0.025 to 0.033%.
  - Drug at a level of 0.1 % in the ration inhibited invasion by the sporozoites.

Cont. ...

Toxicity

- When used at higher dose for long duration it produces toxic effects which include multiple hemorrhages in many organs accompanied by necrotic lesions in the spleen, hypoplasia of bone marrow and agranulocytosis.
- This toxicity is associated with an interference with vitamin K metabolism.
- This compound has 6 days withdrawal pre marketing requirement and eggs from treated birds should not be used for human consumption.

Ethopabate

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Ethopabate

Description

› It is an arylamide containing one phenyl ring, belonging to monocyclic aromatics, is a very safe drug.

Cont. ...

Spectrum

- It has anticoccidial activity especially against intestinal forms.
- It lacks activity against E. *tenella* of caecal worms.
- This drug is a competitor of PABA for absorption by the parasite and interferes with folate synthesis.
- It has good activity against E. *acervulina* and some strains of E. *maxima* and E. *brunette*.

Dosage:

- It has been used only in combination with Amprolium first at 4 ppm and later at 40 ppm.
- This drug has peak activity on 4^{th} day of cycle.

Clopidol

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Clopidol

Description

- It is the only member of its class i.e. pyridinols having useful anti coccidial properties.
- It is also called metichlorpindol or clopindol.

Cont. ...

Spectrum

- It has broad spectrum activity.
- It is almost completely coccidiostatic in action and effects the sporozoites or trophozoites.
- It is most active against the **sporozoite** stage of *Eimeria.*
- Thus to produce full anticoccidial potential, it should be **in the feed of chickens on the day of exposure to coccidial oocyst.**
- Day one of the coccidia cycle is designated as day of peak activity for clopidol.

Cont. ...

- Drug is **not active** if given after day of exposure, so should be given on day first.
- Its coccidiostatic activity holds the sporozoites undeveloped in an epithelial or host macrophages cells for as long as 60 days.
- Latent coccidiosis may appear if drug is withdrawn during the static state, as the parasites resume development.

Cont. ...

Dosage:

- This drug is generally administered at 125 ppm in the feed.
- It may be used in last 1-3 weeks of the broiler grow out.
- There is no premarketing withdrawal requirement.

Quinolones

Quinolones

- There are hundreds of Quinolones which have been synthesized and a number of them have showed activity against various groups of parasites.
- Buquinolate, 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 1st day 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.

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Buquinolate

- It has broad spectrum of activity against all chicken coccidia.
- It arrests sporozoite development but does not kill these forms.
- The inhibited stages may recommence development if it is withdrawn too early.
- It is given at the level of 0.00825% in the feed.
- It favourably increases the feed conversion rates.
- This drug has low toxicity and elimination rate is fast from the tissues following withdrawal of medicated feed.

Decoquinate

- It also has broad spectrum coccidiostat activity and inhibits sporozoite development.
- It is used at a concentration of 0.003% in the feed.
- This compound has no pre marketing withdrawal requirements.

Robenidine

- It is a guanidine derivative.
- It is a broad spectrum coccidiostatic and coccidiocidal drug, used for the prophylaxis of coccidiosis.
- It inhibits oxidative phosphorylation in late 1^{st} and 2^{nd} stage schizonts.
- It may also have an effect on the gametocytes.
- It is most effective against the maturing first generation schizonts.
- It is effective as 0.0066% mixture in the feed.
- 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 before slaughter.

Halofuginone

- Halofuginone is a quinazolinone derivative.
- It is an alkaloid originally isolated from the plant Dichroa febrifuga and tested for antimalarial activity in China many years ago.
- This drug has potent broad spectrum coccidiocidal and coccidiostatic activity against 1st and 2nd generation schizonts.
- The mechanism of action against *Eimeria* spp. is unknown at present.
- It is used for the prevention of coccidiosis and should only be given to young birds (up to 12 weeks of age for poultry).
- The drug is effective against pathogenic eimerian species in chicken at a feed concentration of 3 ppm.
- The drug is not given to the egg laying birds and has 5 days withdrawal period for the slaughter.

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