

Chapter No. 9.

Importance of chemotherapy in relation to parasitic control programme, Anthelmintic medication, Use and abuse of antiparasitic drugs, Insecticides and acaricides, Antiprotozoal drugs in veterinary practice

What is chemotherapy?

It is a branch of pharmacology that deals with the drugs which inhibit the specific organisms or parasites that cause disease **or** It is a branch of pharmacology which studies about the drugs in relation to the treatment of diseases.

Importance of chemotherapy

In a few couple of futuristic essays (Brown, 1978, Oram *et al.*, 1979) it was speculated that, the need for increased food production from an increasingly low agricultural land will be a major challenge particularly in the developing countries during the next few decades, which has come to a reality. In order to produce a large amount of food, more technological investments will have to be put, this includes synthetic and natural chemicals to prevent and control parasitic diseases in animals.

Chemotherapy is the most effective method to control many of the parasitic infections in combination with other supportive measures that are essential for a particular parasitic infections, environment and animal population. Chemotherapy in the ancient days was simple, empirical and based mostly on the use of plants or its products. At present many new safe and efficient chemotherapeutic drugs are available to control many of the parasitic infections.

What is an antiparasitic drug ?

The drug which acts against parasite by killing the parasite or removing the parasite is known as antiparasitic drug.

What is therapeutic ratio?

The ratio between maximum tolerated dose and minimum curative dose is known as **Therapeutic ratio**.

Characteristic of an ideal antiparasitic drug:-

1. The antiparasitic drug should be highly effective.
2. It should have broad spectrum activity.
3. The therapeutic ratio should be high.
4. The mode of administration should be easy.
5. The drug should be stable for a long time.
6. The drug should not be expensive.
7. It should not induce resistance
8. The drug should have no residue in food animals or in milch animals.
9. It should not have side effects either on the patient or its handler.
10. It should not have complex dosing schedule.

What is Rational Therapy?

It is a mode of treatment based on pharmacological actions of drugs in relation to disease.

What is Supportive Therapy?

It is a method of treatment other than drugs for example, high protein during hypoproteinaemia.

Anthelmintic

Anthelmintics are the chemicals used for the prevention and control of trematodes, cestodes, and nematodes

Vermicide

The drugs that kill the worms.

Vermifuge

The drugs use to affect the worm in such a manner that the peristaltic activity or catharsis expels it from the intestinal tract.

Endecticide

Drugs which have activity against both the ecto and endoparasite.

Classification of antiparasitic drugs:-

The antiparasitic drugs can be divided into four groups

(a) Antiprotozoals:

Antiprotozoals are the drugs used for the prevention and control of protozoan parasites like *Babesia*, *Theileria*, *Trypanosoma*, *Leucocytozoon*, *Histomonas*, and *Trichomonas*.

(b) Anticoccidials:

These are the chemicals for the prevention and control of coccidian.

(c) Anthelmintics:

Anthelmintics are the chemicals used for the prevention and control of trematodes, cestodes, and nematodes

(d) Pesticides:

Pesticides are chemicals used for the prevention and control of ticks, flies, fly larvae and fleas.

A) Antiprotozoals:-

Common name	Product name	Indication	Use level (mg/kg body wt.)	Route of therapy
Trypan blue	-	<i>Babesia</i>	2-3	Intravenous(i/v)
<i>N,N'-di-6-quinoliny-urea</i>	Babesan	<i>Babesia</i>	1	Subcutaneous(s/c)
Quinuronium sulfate	Acaprin	<i>Babesia</i>	0.6-1	s/c
Diminazine aceturate	Berenil	<i>Babesia</i>	3.5	Intramuscular (i/m), i/v
Acridiflavine	Gonacrine	<i>Babesia</i>	20ml, 5% solution	i/v
Imidocarb	Imizol	<i>Babesia</i>	1.2-3	s/c, i/m
Amicarbalide diisethionate	Diampron	<i>Babesia</i>	5-10	i/m, s/c
Phenamidine isethionate	Lomadine	<i>Babesia</i>	8-13.5	s/c
Isometamidium chloride	Samorin	<i>Trypanosoma</i>	0.25-2	i/m
Quinapyramine sulfate	Antrycide	<i>Trypanosoma</i>	5	s/c
Suramin	Naganol	<i>Trypanosoma</i>	7-12	i/m
Nitrasone	Histostat	<i>Histomonas</i>	187.5ppm	Feed

Dimetridazole	Emtryl	<i>Histomonas,</i> <i>Trichomonas</i>	100-500 ppm	Feed, water
Clopidol	Coyden	<i>Leucocytozoon</i>	125-250ppm	Feed

For *Theileria* : Tetracycline, Halofuginone, Parvaquone

For other protozoa: Metronidazole, Quinacrine hydrochloride, Mepacrine

Drugs used against Toxoplasmosis: Sulfonamides(Sulfamerazine, Sulfadimidine, Sulfadiazine) in combination with pyrimethamine.

B) Anticoccidials :

Poultry anticoccidials are usually mixed in the ration and fed continuously to prevent disease outbreaks. Some poultry producers change the anticoccidials used in the rations once or twice per year. This procedure is generally referred to as a rotation program, is considered by some to retard the development of resistant coccidia. Others use the rotation programme to lower their drug costs by using less expensive medication during times of the year when coccidiosis outbreaks are not common. The shuttle program is another procedure used by some broiler producers for the same reason as described above. In a shuttle program, one product is used in the starter ration and a second in the finisher ration. When cost reduction is the primary reason for using the program, the least expensive anticoccidial is used in the finisher ration. Some of the poultry anticoccidials are :-

Common name	Product Name	Feed use level Chickens (ppm)
Amprolium	Amprol	125-250 (feed or water)
Amprolium + Ethopabate	Amprol Plus	125 + 4-40
Amprolium+Ethopabate+Sulfadimethoxine	Pancoxin	25 + 5 + 60
Clopidol	Coyden	125-250
Monensin	Coban	100-125
Nicarbazin	Nicarb	100-200

C) Anthelmintics:

Anthelmintics are the chemicals used for the prevention and control of trematodes, cestodes, and nematodes.

Characters of effective anthelmintic drug:

1. The anthelmintic should reach the target area where the worms are located.
2. The anthelmintic should not cause irritation to the gastrointestinal tract and should not produce diarrhea, nausea, vomition.
3. They should not be absorbed from the gut when used against the gut worms,
4. The drugs should be absorbed by the body when used against the tissue worms and there should not be any systemic toxicity.

i. Antitrematodal drugs:-

Antitrematodal drugs are used against trematode parasite. They are also known as flukicides. The primary objective of flukicide therapy should be to reduce the number of flukes in the host and to limit deposition of fluke eggs on pasture. This normally requires several treatments per year. The timing of the therapy depends upon the seasonal pattern of infection in grazing animals, the availability and use of snail infested grazing areas, and the general level of infection in a herd or flock. Therapy is generally recommended in conjunction with other control measures such as the use of molluscicides(drugs that kill snails) drainage of snail habitat, and the application of grazing management practices designed to reduce contamination of snail habitats with fluke eggs. Following are the common antitrematodal drugs used in veterinary practice :-

Common name	Product name	Dose rate (mg/kg)	
		Cattle	Sheep
Nitroxylin	Trodax	8-10 (s/c)	12-15 (s/c)
Oxyclozanide	Zanil	10-15(suspension., orally)	15-20(suspension., orally)
Rafoxanide	Ranide	7.5- 10 (suspension., orally)	7.5-15(suspension., orally)
Carbon tetrachloride	Many	Not indicated	80 (oral, i/m, s/c)
Hexachloroethane	Many	300(suspension., orally)	300(suspension., orally)
Hexachlorophene	Many	15(suspension., orally)	15(suspension., orally)
Albendazole	Albomar	15(suspension., orally)	7.5-15(suspension., orally)
Praziquantel	Droncit	30(suspension., orally)	30(suspension., orally)
Triclabendazole	Fasinex	5-15 (tab, orally)	5-15(tab, orally)

ii. Anticestodal and Antinematodal drugs:

The chemotherapy of helminth parasites entered a new era in the 1960 with the development of the benzimidazole, imidazothiazole, organophosphate, and tetrahydropyrimidine anthelmintics. These chemicals groups provided improved efficacy, broader spectrum and greater safety in comparison with older drugs. A greater variety of formulations were also developed to facilitate treatment. Therapy may now be given by oral drench , drinking water , bolus, feed top dressing , feed supplement medicated mineral block , or protein cube, parenteral injection, external application by pour on or spot on and most recently , paste or gel formulations.

The objective of anthelmintic therapy is to :-

- a) Eliminate or at least reduce to acceptable levels the existing helminth infections.
- b) To prevent or reduce the build-up of parasite eggs and ultimately, infective stages in the host's environment.
- c) To prevent infection by prophylaxis, to prevent and cure outbreaks of disease
- d) To improve animal performance
- e) To facilitate the development and maintenance of immunity.

The conventional and routine approach to the control of helminth parasites in animals is to administer a therapeutic dose of an anthelmintic several times per year. The frequency and timing of treatment varies depending upon the host species, infection, local customs, and anthelmintic costs. Therapeutic treatment is normally given as a single dose, but programs have been developed with some anthelmintics, e.g. fenbendazole and mebendazole in which the therapeutic dose is subdivided into 5 to 21 daily doses. This gives the veterinarian and livestock owner more flexibility in applying anthelmintics.

Anthelmintic Chemoprophylaxis

The chemoprophylactic use of anthelmintics is an alternative to conventional programs of therapy. In a chemoprophylaxis program, the anthelmintic is given continuously for some preselected period to prevent infection. The anthelmintic may be given in the feed, water, mineral supplement, or a sustained release bolus. Ideally, the program should protect the host from the potential deleterious effects of the larval stages and development of mature stages. Consequently, the significantly, fewer worm eggs are deposited in the environment, and disease producing levels of infective-stage eggs or larvae do not occur. Both pyrantel tartrate and morantel tartrate are used in chemoprophylactic programs for pigs and cattle, respectively.

Following drugs are used in anthelmintic chemotherapy against nematode and cestode parasites:-

Common name	Product name	Indication	Dose rate (mg/kg)			
			Ruminants	Horses	Pigs	Chickens
<i>Benzimidazole</i>						
Albendazole	Albomar	GI, L,T	5-7.5	3-5	N	N
Fenbendazole	Panacur	GI, L,T	5-7.5	7.5-60	5-25	N
Mebendazole	Mebex	GI, L,T	12.5	5-10	6	50
Parbendazole	Helatec	GI	20-30	5	30	N
Thiabendazole	Thibenzole	GI	44-110	45-90	50-100 50-1000 ppm in feed	1000ppm
<i>Imidazothiazole</i>						
Tetramisole	Nilverm	GI, L	15	N	15	40
Levamisole hydrochloride	Levasole	GI, L	15	N	7.5	25
<i>Organophosphates</i>						
Coumaphos	Baymix	GI	8-15 (feed)	N	N	30-40 ppm
Dichlorvos	Atgard	B,GI	N	40	40	N
<i>Tetrahydropyrimidines</i>						
Morantel	Banminth II	GI	10	10	10-25	N
Pyrantel tartrate	Banminth	GI	25	12.5	10-25	N
Pyrantel pamoate	Nemex	GI	N	19	N	N
<i>Miscellaneous</i>						
Diethylcarbamazine	Franocide	L	44 or 22 X 3 days			N
Ivermectin	Ivomec	GI, L	200µg/kg s/c, oral	200µg/kg, i/m	N	N
Niclosamide	Yomesan	T	70-100	200-300	N	100-200
Phenothiazine	Many	GI	200-600	66	N	0.5g/bird

Piperazine	Many	GI	N	100-200	110	300
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B: Horse bot; GI: gastrointestinal nematodes; L: Lungworms; T: Tapeworms

i/m : Intramuscular; s/c : Subcutaneous;

D. Pesticides

I. Insecticides(used against the insects):

Drugs which are used against the ectoparasite are known as pesticides or ectoparasiticides.

II. Acaricides :

Drugs which are used against arachnids such as ticks and mites are known as acaricides.

Large animals and birds are infested with a variety of external parasites., including ticks, mites, lice , adult flies, fly larvae, mosquito , and fleas. The clinical importance of these infestations and impact on production economics depends on many factors such as the species of parasites involved and whether the parasite is a vector of protozoal, rickettsial, bacterial, or viral organisms. Pesticides provide an easy and relatively inexpensive way of controlling ectoparasites. The most common method of pesticides application are dipping, spraying, pour on and dusting, .Special methods include the use of back rubbers impregnated with pesticide, feeding in a supplement to control larvae in the manure, and resin ear tags impregnated with pesticide.

One of the most efficient methods to treat large numbers of animals is by total immersion in dipping vats containing the pesticide at the recommended concentration. It is important to maintain the proper concentration of pesticide in the dip. Dipping vats designed to insure animals enter one at a time and that upon emergence, fluids draining from the animal will flow back to the vat. Spraying animals in spray races, showers or by portable sprayer is somewhat less efficient. The operators must be thorough in applying the pesticides and careful in maintaining the equipment to insure proper operation. The pour on method of application in

which the pesticide is applied in high concentration and low volume along the middle of the back, is effective with those pesticides which act systematically by absorption through the skin. Dusts are effective for the control of some external parasites such as lice and ear ticks. They are applied by hand or in various types of dusting containers. Many pesticides are used as sprays, dusts or in resin strips in or around animal buildings to control parasites off the host. The frequency of treatment varies and is influenced by many factors, including the seasonal Occurrence of the different kinds of ectoparasites, the type of pesticide in use, and management practices. A tick control program for complete control of a three –host tick may require, for example immersion every 4th day where some larvae, nymphs and adults are present throughout the year.

Characters of an ideal pesticide:-

1. It should destroy all ectoparasite at every stage of their life cycle
2. It should be rapid in action.
3. It should be non-toxic or less toxic to the host.
4. It should be economical
5. It should be compatible with the various bases and vehicles required for application.
6. It should provide a minimum residue in or on the host and be rapidly detoxified in the environment.

Following pesticides are in use:-

Common name	Product name	Indication	Host species	Application
<i>Organophosphates</i>				
Coumaphos	Asuntol	Ticks, lice keds, fleas, blowflies, ox warb;e, flies, screwworms	C/Ch/H/P/S/G	dip, spray, back rubber, dust,, pour on
Malathion	Cythion	Tick ,lice, mite,flea, flies, keds	C/Ch/H/P/S/G	Spray, dip, dust
<i>Carbamate</i>				
Carbaryl	Sevin	Tick, lice, mite, flies, fleas	C/Ch/H	Dip, spray, dust
<i>Organochlorine</i>				
Lindane	Many	Tick, lice, mite, flies, keds	C/P/S/H/G	Spray back rubber ,dust, pour on , dip
Toxaphene	Toxaphene	Tick, lice, mite, fly, bnlow fly, ked, skin bots,	C/P/S/G	Dip, spray, dust back rubber
<i>Diamidines</i>				
Amitraz	Taktic,	Ticks	C	Dip, spray
Chlormethiuron	Dipofene	Tick	C	Dip. Spray
<i>Miscellaneous</i>				
Cypermethrin	Curatick	Tick	C	Dip
Ivermectin	Ivomec	Mite, lice, ox warble, stomach bots	C/H	s/c, i/m, oral

Pyrethrum	Many	Fly, flea, kid, lice	C/S/G/P/Ch	Spray
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C: Cattle; Ch: Chicken; P: Pig; H: Horse; G: Goat , s/c : Subcutaneous; i/m : Intramuscular

Use and abuses of antiparasitic drugs in veterinary practice:

Every drug which is used to control the parasitic diseases has some advantages when used in a proper way and in recommended doses and disadvantageous when not used in proper way as recommended doses in veterinary practice.

Use :

In the recent years, good progress has been made in the development of newer and effective drugs for the treatment and prevention of many parasitic diseases of veterinary importance. This will happen due to increased understanding of the basic physiology, biochemistry, and molecular biology, of the parasites, and the interactions of the parasites with the host. The availability of two or more drugs against parasitic infection or infestations has offered the advantage of the choice of a relatively safe and more effective drug for the treatment of the parasitic infection/infestations.

Abuse:

It is an important fact that no drug is completely harmless. It may be poisonous if doses and the route of entry into the living organisms are not restricted.

References

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