The name helminth was primarily used to denote the worms of the phyla platyhelminthes and nemato helminthes, but has acquired a wider sense, being now generally used for worm parasites, and include the groups platy helminthes (Tape worms, flukes), nemato helminthes (horsehir worms), acanthocephala (thread worms) and annelida (leeches).

The term worm\textsuperscript{[1]} is loosely applied to an assemblage of organisms with elongated bodies and more or less creeping habit. These phyla\textsuperscript{[2]} occupy an important position in the animal kingdom. In 1947 sto\textsuperscript{[3]} estimated that around 400 million helminthes occur in among some 2,000 million people. There is enough reason to believe that the number of people with helminth infections has increased considerably.

Helminths cause mechanical damage by biting intestinal wall and causing haemorrhages (hook worms), tumors (schistosomes and spirurata, peforate) and cause peritonitis of walls of digestive tract. Tissue damage and inflammation due to burrowing is caused by lung flukes and guinea worms. Some cause loss of blood, anaemia and Vitamin deficiency ex.dibothrioce phalus cause B\textsubscript{12} deficiency. Some block passages and cause obstruction ex. ascaris, liver flukes and bancrofts filarial and they interfere with the normal flow of lymph, bile etc. Some cause eosinophilia, carry pathogenic bacteria, allergic reactions (migrating larvae, guinea worms etc.). These allergic reactions give rise to the symptoms of helminth infections. Helminths\textsuperscript{[1]} cause a variety of diseases. Domestic animals also carry the burden of parasitic worms. The main parasitic worms of India are round worms, hookworms, thread worms, tapeworms, guinea worms, filarial worms and flukes which come under nematodes, cetodes and trematodes.

The infections of helminths are wide and cause number of diseases in man and animals. Most worms are harmless free living organisms but some of them are parasites and may do harm to their host in the following ways.
1. By absorbing food (tape worm) or sucking food (hook worms).
2. They feed on the tissues of the host (ascarids) and damage them (\textit{cysticerus tenicollis}).
3. Also by causing mechanical obstruction or pressure (ascarids) and causing wounds through which infection may enter (ascaris).

4. By secreting toxins or other harmful substances.

5. By transmitting the causal agents of infectious diseases such as bacteria, rickettsiae, viruses, protozoa, filariae, and spirochaete and there are some more ways by which they cause much concern to human being.

The brief account of different types of common helminth diseases and drug\(^{[4-7]}\) used for them are given below.

1. **Ancylostomiasis**

   It is caused by an intestinal infection in man by two hookworms – *Ancylostoma duodenale* and *Necator americanus*. The disease is found in tropical and subtropical countries. Man acquires infection when the filarial worm larvae penetrate through the skin of hand and feet. They develop in small intestine. Infections results in gastrointestinal disturbances like anaemia and nervous disorders. **Drug**—Tetra chloroethylene and carbon tetrachloride are effective.

2. **Ascariasis**

   It is a roundworm infection\(^{[8]}\) caused by *Ascaris lumbricoides*. Infection causes with contaminated food and water. It lives in small intestine of man, certain apes and pigs. About 16% of the population of country is affected by ascariasis. Worms in intestine cause abdominal pain, headache and vomiting. **Drug** — Piperazine salts are most useful.

3. **Trichuriasis**

   It is a whipworm infection caused by *Trichuris trichura*, which occurs in man and pigs. It resides in the large intestine. Infection in human results from the ingestion of ova from faecally polluted soil. It was common in warm climate. Loss of appetite and diarrhoea may occur.

4. **Enterobiasis**

   It is commonly called pinworm infection caused by *Enterobius Vermicularis*. This kind of infection is most common in children. It's larval forms mature in the ileum. The worms cause irritation, loss of appetite, sleeplessness and nervousness.
**Drug:** Piperazine is the drug of choice in enterobiasis.

5. **Strongyloidiasis**

   This is most frequently acquired by penetration of the skin by the larva of *Strongyloides stercoralis* commonly called thread worms. These invade the lining of the alimentary canal.

**Drug:** Drugs used are dithiazine.

6. **Trichinosis**

   Trichinosis is caused by *Trichinella spiralis*. These occur in small intestine of man, pig, rat and many other mammals. Infection is acquired by eating raw or improperly cooked pork.

**Drug:** Piperazine citrate.

7. **Taeniasis**

   It is a tapeworm infection caused by the species belonging to the genus *Taenia* which include mainly *Taenia solium* and *T. saginata*. Infection is acquired by eating improperly cooked pork.

**Drug:** Commonly antimalarial drugs are used.

8. **Schistosomiasis**

   It is caused by three species of blood flukes. *Schistosoma mansoni*, *S. japonicum* and *S. haematobium*. These live in blood streams.

**Drug:** Antimony compounds are used.

9. **Fasciolopsiasis**

   It is caused by Intestinal fluke *Fasciolopsis Foelleborni*. It causes erosion of intestinal lining, resulting in bleeding and pain.

**Drug:** Hexylresorcinol and crystaloides are helpful.

10. **Fascioliasis**

    It is caused by liver fluke *Fasciola hepatica*. It usually inhabits the liver and bile duct of cattle, sheep, rabbit and also other vertebrates. It damages the liver as well as bile duct of the host and causes the diseases called liver-rot or *fascioliasis*.

**Drug:** Hexachlorothane and CCl₄ are effective.
11. **Paragonimiasis**

This disease is caused by lung fluke, *Paragonimus westermani* and results in chest pains and shortness of breath.

**Drug:** Emetine hydrochloride and sulpha drugs are effective.

12. **Filariasis**

It is caused by filarial worms *Wuchereria bancrofti* and *w. malayi*. These worms live in the lymphatic vessels and connective tissues of the body. Infection is acquired through the bites at culex mosquito. This disease disfigure legs and other parts of the body and are enormously enlarged called elephantiasis.

**Drug:** Hetrazan

Earlier number of workers\(^9\)\(^{-11}\) have reported the anthelmintic activities of a large number of plant products as well as synthetic compounds and found many of them possessed good anthelmintic activities. Recently some compounds like triazolothiadiazines\(^12\)\(^{-13}\) quinozolines\(^14\) heterocyclic compounds\(^15\) and \(s\)-substituted phenothiazine\(^16\) and piperazine have been suggested as good potential anthelmintic agents.

The chemotherapeutic anthelmintics destroy the parasitic worms or remove them from hosts either the way of:

1. Direct action on the worm causing paralysis or death.
2. By irritating the tissue of the parasite.
3. Antimetabolic interfering with the metabolisms of parasite.

An ideal anthelmintic\(^17\) should have a broad spectrum of action. It should first paralyse the worm and then expel it. It should achieve a high percentage of cure with a single therapeutic dose. It should be free from toxicity to the host and should be cheap. But at present only a few anthelmintic drugs meet all requirements of a good anthelmintic agent.
CLASSIFICATION

Anthelmintics may be classified in two different ways.

A. According to their mode of action

(i) Vermicides are drugs that paralyse or kill parasites.
(ii) Vermifungus are drugs that weaken the worms so that they can no longer attach themselves to the intestinal mucosa and thus can be expelled.

B. According to their chemical structure

(i) Chlorinated hydro carbons – CCl₄, tetrachloroethylene, etc.
(ii) Phenols and related compounds – thymol (oil of thyme), hexylresorcinol.
(iii) Antimonials and arsenicals – stibophen, tartaremethine.
(iv) Piperazine derivatives – hetrazan, antepar.
(v) Triphenyl methane cyanine dyes – gentin violet, crystal violet.
(vi) Phenothiazines, certain antimalarials (azacrine), certain xanthenes, carbamates.
(vii) Natural products – pelletierine, santonin, oil of chenopodium, aspidium, and emetin.

Vegetable remedies like malefern, cusso, arecanut (tape worms) and santonin (nematods) are the earliest known anthelmintics. In 1880 a landmark was set when the value of thymol for hook worms was established by some Italian workers. Other anthelmintics were oil of chenopodium [1913], CCl₄, [1921] tetrachloroethylene [1925], hexylresorcinol [1930], replaced oil of chenopodium in ascariasis. McDonagh and christopherson established the value of antimony compounds for schistosomiasis. Gentian violet [1927] was replaced by chloroquine for clonorchis, Piperizine for enterobius and dithiazone for strongyloides. Phenothiazine [1938] by Harwood and hexachloroethane [1926] for Fasciola were discovered. After world war II, aterbin (for tape worms), antimony and arsenic compounds and hetrazan (for filariasis) were introduced. After world war II, piperazine salts played vital role as anthelmintics (i.e.) hetrazan is useful against a number of helminthes.
MODE OF ACTION

Anthelmintics are the drugs used in the treatment of helminthiasis. They are used to kill or remove the parasitic worms and rid the host of them. An ideal and effective anthelmintic drug\textsuperscript{[22]} is one that causes minimum toxicity to the mucous membrane of gastrointestinal tract and alimentary tract, if absorbed from it. Drug should be chemically stable, inexpensive and tolerable orally without producing symptoms. Most important is that the drug should reach that portion of the intestine where the worm infestation occurs with minimal degree of absorption. It should be immediately lethal. Anthelmintic causes death or remove the worm by stimulating paralysis or nacrosis. This is accomplished by gaining access into the body via cutile or ingestion and interfering with worms metabolism. It should be specific.

EVALUATION OF TECHNIQUE

In vitro techniques involve \textit{A. lumbricoides, Unicara stercencephala} and some other species of worms. Very few helminthes of man infect the laboratory animals. The condition of alimentary canal of different experimental animals may not be the same. So the screening of anthelmintic activity may be done by exposing the worm to the solution of anthelmintic substances.

In has been reported by sollman\textsuperscript{[23]} that all clinical anthelmintics are toxic to earth worms. Trandelberg proved that various species of ascaris have remarkable anatomical similarities with common earthworms. Furthermore a number of workers\textsuperscript{[24-32]} have used earthworms for preliminary, in vitro, evaluation of anthelmintic activity of new substances. Due to the availability of earth worms and their acceptance as substitute, qualitative in vitro anthelmintic screening of synthesized heterocyclic compounds, was done using earth worms by adopting the technique given by Watkins\textsuperscript{[33]}.

METHODS AND MATERIALS

4 and 2 percent solution of 1,4- dihydro pyridines, pyrimidiens, pyrazines 2-pyrazolines and 4-thiazolidiniones were prepared in ethylene glycol. Same concentrations (4 % and 2 %) of standard drug piperazine hydrochloride was also prepared in ethylene glycol.
In the petridish, 25ml. normal saline solution and 2ml of test sample solution were poured. Two living earthworms of nearly equal size, washed with normal saline solution were transferred into the petridish. Same experiment was performed with the standard.

The time taken by earthworm to become motionless was noted as paralytic time. The time of death is noted as lethal time. Death of motionless earthworm was ascertained by placing the earthworm in like warm water, which stimulates movement if the worm is alive. Experiments were carried out in duplicate and average values are shown in the form of graphs. The blank experiments with only ethylene glycol showed no activity and the earthworms were active even after 100hrs.
GRAPH I: ANTHELMINTIC ACTIVITY OF 1,4-DIHYDRO PYRIDINES
GRAPH II: ANTHELMINTIC ACTIVITY OF PYRIMIDINE-2-THIONES/ONES

Compound Code
2% Concentration Solution Graph
- Paralytic time □ Lethal time

Compound Code
4% Concentration Solution Graph
- Paralytic time □ Lethal time
GRAPH III: ANTHELMINTIC ACTIVITY OF 2-THIOLS/OLS

Compound Code
2% Concentration Solution Graph
▪ Paralytic time □ Lethal time

Compound Code
4% Concentration Solution Graph
▪ Paralytic time □ Lethal time
GRAPH IV: ANTHELMINTIC ACTIVITY OF PYRAZINES

Compound Code
2% Concentration Solution Graph
- Paralytic time
- Lethal time

Compound Code
4% Concentration Solution Graph
- Paralytic time
- Lethal time
GRAPH V: ANTHELMINTIC ACTIVITY OF 2-PYRAZOLINES

Compound Code
2% Concentration Solution Graph
- Paralytic time - Lethal time

Compound Code
4% Concentration Solution Graph
- Paralytic time - Lethal time
GRAPH VI: ANTHELMINTIC ACTIVITY OF 4—THIAZOLIDINONES

[Bar charts showing paralytic and lethal time for various compounds labeled by code and concentration (2% and 4% solutions).]
RESULT AND DISCUSSION

In 1, 4-dihydropyrimidines the methoxyphenyl and chlorophenyl shown more activity than the rest. In pyrimidine group chlorophenyl and furyl derivatives more active. In pyrazine series 4-hydroxy-3-methoxy phenyl derivatives exhibited more potency. In 2-pyrazoline series methoxy phenyl and chlorophenyl derivatives showed more activity. In the 4-thiazolidinone series 4-hydroxy-3-methoxy phenyl showed more activity.

SUMMARY

Watkins method was adopted in evaluation of the anthelmintic activity. 4% and 2% solutions synthesized heterocyclic compounds were prepared in ethylene glycol. In the petridish, 25ml normal saline solution and 2ml of tests samples solutions are poured. Two diving earth worms of nearly equal size, washed with normal saline solution, are transferred into petridish. Same experiment is performed with the standard. The time taken by earthworms to become motionless was noted as paralytic time. The time of death is noted as lethal time. p-methoxy phenyl, p-chloro phenyl derivatives showed good activity.
REFERENCE

21. Tullio Bacchetti, "Chem Abstr.", 52, 256v (1960);