Q. Write a note on antiamoebic agents

→

Antiamoebic agent or amebicide is an agent that is destructive to amoeba, especially parasitic amoeba that cause amoebiasis.

Amoebiasis (or amebic dysentry) is an infection of intestinal tract caused by species of Entamoeba (E. histolytica and E. dispar)

The disease can be acute or chronic, with the patients showing varying degrees of illness, from no symptoms to mild diarrhoea to fulminating dysentery.

The therapy is aimed not only at acutely ill patients but also at those who are asymptomatic carriers, because dormant E. histolytica may cause future infections in the carrier and be a potential source of infections for others.

This disease is classified as follows:

I Asymptomatic
II Symptomatic
a) Intestinal Amoebiasis
(i) Dysentery
(ii) Non dysenteric colitis
(iii) Amoeba
(iv) Amoebic appendicitis.

b) Extraintestinal amoebiasis
(i) Hepatic acute non suppurative
(ii) Liver abcesses
III Cutaneous involvement of other organs

Entamoeba histolytica exists in two forms:
- Cystes form
- Trophozoites form

Life cycle of amoeba consist of following steps:
1 Ingestion of cysts
2 Formation of trophozoites
3 Penetration and multiplication of trophozoites
4 Systemic invasion
5 Cysts discarded

• Classification of antiamoebic agents.

I According to site of action

1 Luminal amoebicides:
It is active only against intestinal forms of amoeba

2 Systemic amoebicides:
These agents primarily use to treat severe amoebic dysentery or hepatic abscesses.

3 Mixed amoebicides:
These agents are active against both intestinal and systemic forms of amoeba

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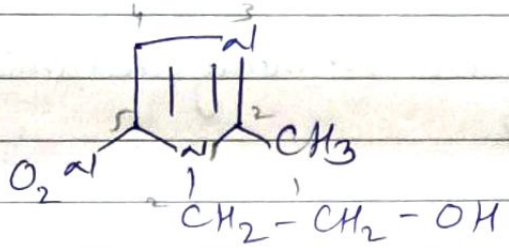
I Tissue amoebicides

1 For both intestinal and extraintestinal amoebiasis

nitromidazoles
Eg: Metronidazole ☆
Tinidazole
Ornidazole

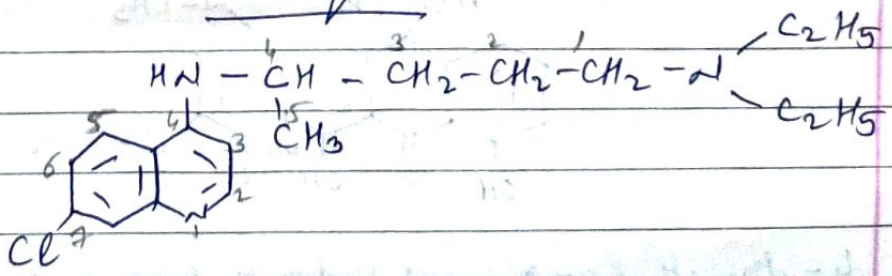
☆ Metronidazole



2-[2-methyl-5-nitro-1H-imidazol-1-yl] ethanol

2 For extra intestinal amoebiasis only
Eg: Chloroquine ☆
Emetine
Dehydroemetine

☆ Chloroquine



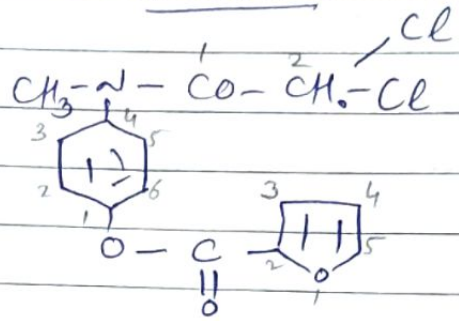
N'-(7-chloroquinolin-4-yl)-N,N-diethyl-pentan-1,4-diamine

II Luminal amoebicides

1 Amide

Eg: Diloxanide * furoate
Nitazoxanide

☆ Diloxanide



4-[2,2-dichloro-N-methylacetamido] phenyl furan-2-carboxylate

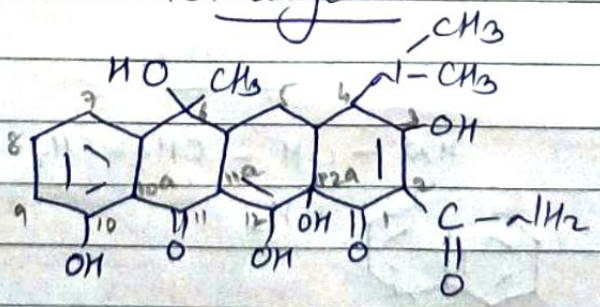
2 8-hydroxyquinolones.

Eg: Iodoquinol * (Diiodohydroxyquin)
Quiniodochlor (Iodochlorohydroxyquin)

3. Antibiotics

Eg: Tetracyclines

☆ Tetracycline



4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacene carboxamide

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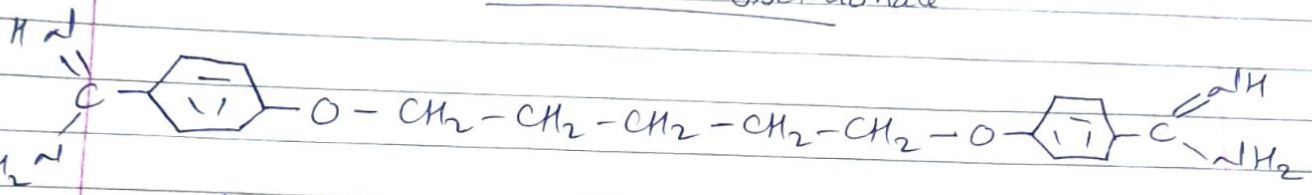
III. Miscellaneous agents
Eg: Pentamidine Isethionate *
Atovaquone
Eflornithine

* Pentamidine Isethionate



4,4' [pentan-1,5-diyl bis (oxy)] dibenzyl carboximidamide

- Uses:
  - In treatment of intestinal and hepatic amoebiasis
  - Used to treat amoeba infection.
  - Pentamidine is an antimicrobial medication used to treat African trypanosomiasis., pneumocystis pneumonia.

- Side effects:
  Headache, Nausea, Vomiting, Abdominal discomfort, Loss of appetite.

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Q Write in detail about anthelmintic agents.

→

Anthelmintics agents are used to treat parasitic infection due to worms.

Helminth means worms.

Helminthiasis is an infections caused by parasitic worms.

The helminths are macroscopic, multicellular organisms, having their own digestive, excretory, reproductive and nervous system.

Helminths are of three types:

- Nematodes (round worms)
Ascarids (Ascaris), filarias, hookworms, pinworms (Enterobius) and whipworms (Trichuris trichiura).

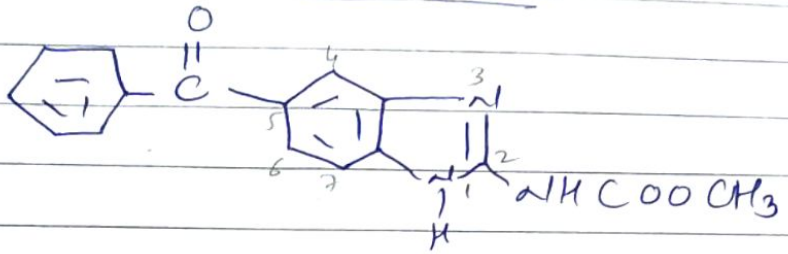
- Cestodes (tape worms)
Multiple species of flat worms, Taenia saginatum, Taenia Solium, Hydatid.

- Trematodes (fluke worms)
Liver flukes, lung flukes, schistosoma (blood flukes), Intestinal flukes.

Classification:

I Benzimidazoles
Eg: Mebendazole ☆
Albendazole
Cyclobendazole

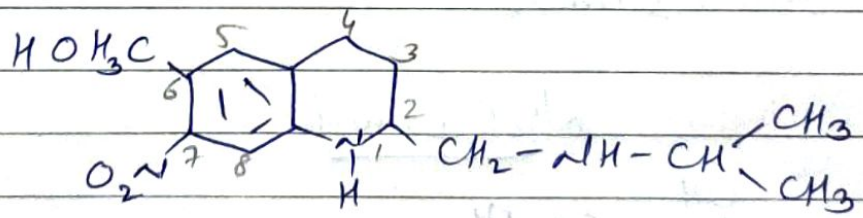
☆ Mebendazole



Methyl -5- benzoyl benzimidazol-2-yl carbamate.

II Quinolones and isoquinolones ☆
Eg: Oxamniquine
Praziquantel

☆ Oxamniquine

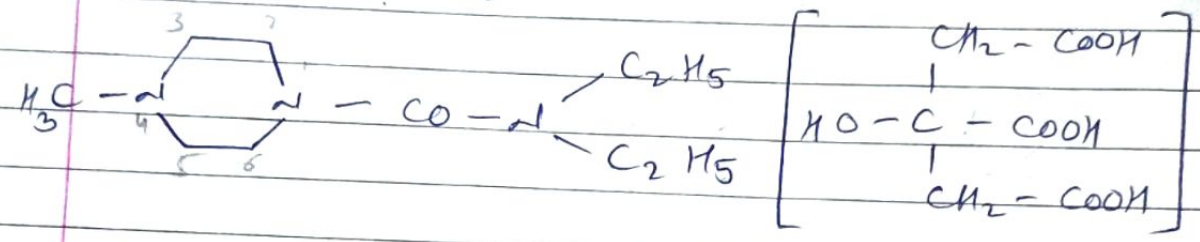


{2-[(isopropylamino)methyl]-7-nitro-1,2,3,4-tetrahydroquinolin-6-yl}methanol

III Piperazine derivatives.
Eg: Piperazine citrate
Diethyl carbamazine

IV - Vinyl - pyrimidines

☆ Diethyl carbamazine

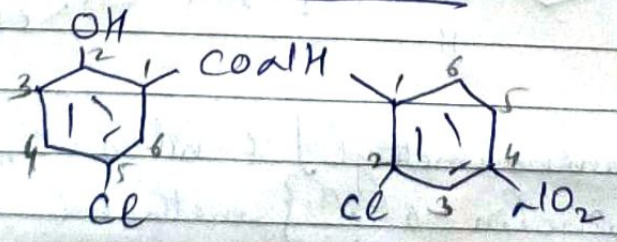


N, N - diethyl - 4 - methyl - piperazin - 1 - carboxamide citrate

IV Vinyl pyrimidines.
Eg: Pyrantel pamoate
Oxantel

V Amides
Eg: Niclosamide

☆ Niclosamide



5 - chloro - N - [2 - chloro - 4 - nitro phenyl] 2 - hydroxy benzamide

VI Natural products
Eg: Ivermectin
Avermectin

VII Organo phosphorus
Eg: Metrifonate

VIII Imidazothiazoles.
Eg: Levamisole

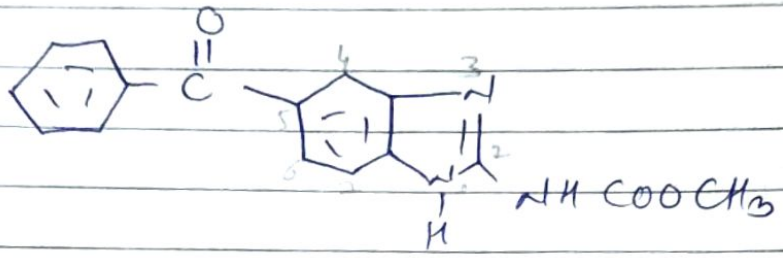
IX Nitro derivatives
Eg: Niridazole

- **Uses:**
  - In treatment of infections by whipworm, pinworm, hookworm, roundworm
  - Also in thread worm infections.
  - In tapeworm infestations, neurocysticercosis, schistosomes.

- **Side effects:**
  - Headache, nausea, vomiting, Fever
  - Hairfall, dizziness, rash
  - Anaemia, acute liver failure, acute renal failure.

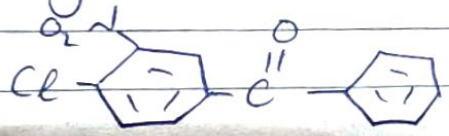
Q IUPAC name, synthesis and mechanism of action of:

1 → Mebendazole



methyl-5-benzoyl benzimidazol-2-yl carbamate

Synthesis

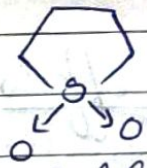


+ NH_4OH

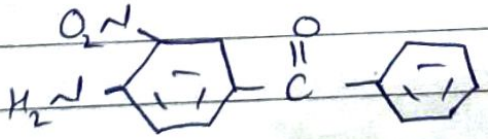
4-chloro-3-nitro benzophenone

Δ 25°C for 24 hrs

CH_3OH ,

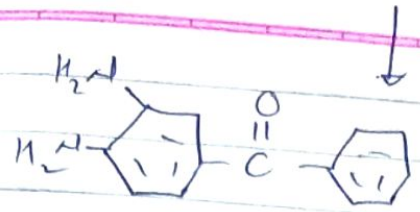


Sulpholane



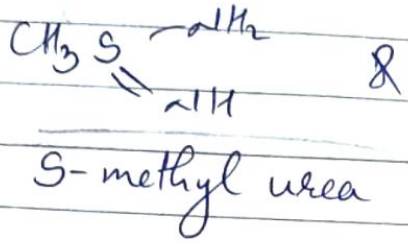
4-amino-3-nitro benzophenone

$HCl + H_2$ gas (Pd on charcoal)



+ HCl

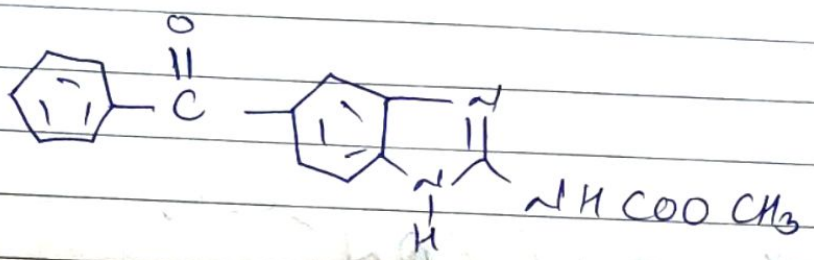
Diamino benzophenone



&

S-methyl urea

HCl $COOCH_3$
Methyl chloro formate
Δ 0-5°C



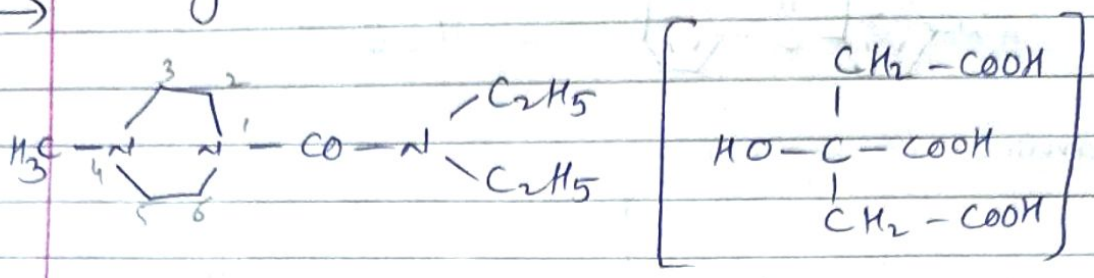
Mebendazole

MOA:

- It act by inhibiting microtubule synthesis.
- It bind with parasite 'β-tubulin' and inhibit it's polymerization.
- In addition probably blocks glucose uptake in parasite and depletes its glycogen stores

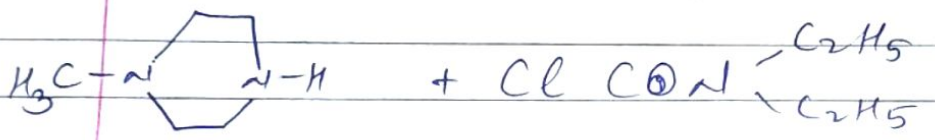
2 Diethylcarbamazine citrate

→



N, N - diethyl - 4 - methyl - piperazin - 1 - carboxamide citrate

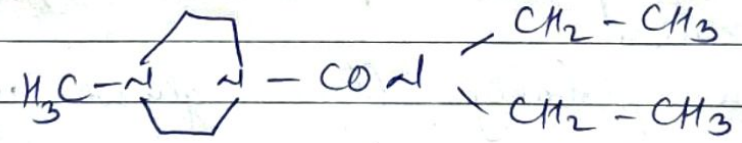
Synthesis



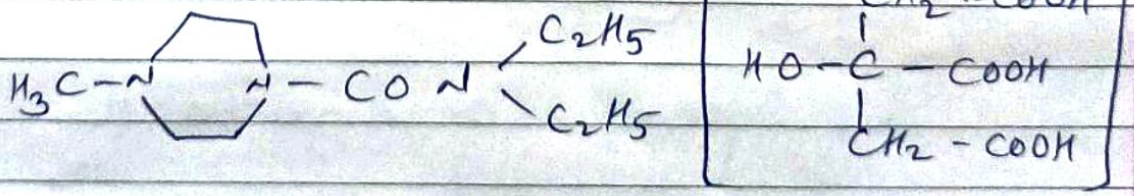
N - methyl piperazin

Diethyl carbamoyl chloride

↓ - HCl



↓ Citric acid



Diethyl carbamazine citrate

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MOA

It act as microfilaricidal by blocking cycloxygenase pathway in parasites.
So, it alters the microfilarial membranes so that they are readily phagocytosed by the tissue bound monocytes.