MATRIC NO ; 16/MHSO6/067.

COURSE TITLE; Introductory Pharmacology and Toxicology II

COURSE CODE; PHA 302

ASSIGNMENT.

BACTERIAL PROTEIN SYNTHESIS INHIBITORS.

1. Write on a named bacterial protein synthesis inhibitor, stating its mechanism of action , indication for use, toxicity and adverse effects.

ANSWER.

1. LINCOMYCIN;

Lincomycin is an antibiotic that is used to treat severe bacterial infections in people who cannot use penicillin **antibiotics**

Lincomycin is used only for a severe infection. lincomycin will not treat a [**viral infection**](https://www.drugs.com/condition/viral-infection.html) such as the [**common cold**](https://www.drugs.com/cg/safe-use-of-cough-and-cold-medicines.html) or flu. Lincomycin (Lincocin) is an injectable man-made antibiotic. Lincomycin kills bacteria by interfering with the ability of bacteria to produce important proteins necessary for them to survive. Lincomycin is effective against many types of bacteria including [*Staphylococcus aureus*](https://www.medicinenet.com/staph_infection/article.htm)*,*[*Streptococcus*](https://www.medicinenet.com/streptococcal_infections/article.htm)*pneumoniae,*[*Streptococcus*](https://www.medicinenet.com/strep_streptococcal_throat_infection_quiz/quiz.htm)*pyogenes, Propionibacterium acnes*, and others.

MECHANISM OF ACTION

**Lincomycin** inhibits bacterial protein synthesis by binding to the 23S RNA of the 50S subunit of the bacterial ribosome. **Lincomycin** is predominantly bacteriostatic in vitro.

INDICATION OF USE .

. Serious infections due to sensitive gram-positive organisms (staphylococci, including penicillinase-producing staphylococci, streptococci and pneumococci) when the patient is intolerant of, or the organism resistant to other appropriate antibiotics .

TOXICITY

Acute toxicity

Lincomycin was toxic in mice and rats when administered

parenterally and was practically nontoxic after oral administration.

Lincomycin was toxic to rabbits by all routes of administration.

*Mice*

The acute LD50 in male mice treated orally was determined for

USP grade and Premix grade lincomycin (Buller, 1979). No significant

difference between the LD50 values of 20 000 and 17 000 mg/kg bw was

determined in this non-GLP study. An LD50 value of 210 mg/kg bw was

measured in mice treated intravenously, and the signs of toxicity in

the survivors included severe sedation lasting 1-2 min (Gray &

Highstrete, 1963a).

*Rats*

The acute toxicity of lincomycin was determined in a preliminary

non-GLP study in newborn and adult rats treated by subcutaneous

injection (Gray & Purmalis, 1962a). The LD50 in newborn rats was 780

mg/kg bw, while that in adults was 10 000 mg/kg bw. An intravenous

injection was reported to be more toxic, with an LD50 of 340 mg/kg bw

(Gray & Highstrete, 1963a).

The acute toxicity of agricultural-grade lincomycin (Glenn &

Garza, 1971) and of USP-grade lincomycin (Brown, 1977a,b) was

determined in a series of non-GLP studies in Sprague-Dawley rats.

Lincomycin was administered orally to groups of five animals of each

sex at doses of 5000-16 000 mg/kg bw, and clinical signs and body

weights were monitored for 2 weeks after treatment. All doses resulted

in clinical signs of toxicity including diarrhoea and ataxia.

Depression was observed at doses > 8000 mg/kg bw, and death,

preceded by coma, was observed at doses of 12 500 and 16 000 mg/kg bw.

While there was no significant effect on body-weight gain, the

survivors continued to have diarrhoea for up to 36 h after treatment.

The LD50 was determined by probit analysis to be about 15 000 mg/kg

bw for USP lincomycin and 11 000 mg/kg bw for the agricultural-grade

product. In a separate study, an LD50 of 16 000 mg/kg bw was

determined for a premix grade preparation of lincomycin (Nielsen,

1975).

*Rabbits*

Rabbits have been shown to be quite sensitive to orally

administered lincomycin (Gray et al., 1965a). After a single

intravenous injection of 0.5 mg/kg bw, 5 out of 10 rabbits either died

or were killed for humane reasons within 2 weeks of dosing, and 7 out

of 10 rabbits had died by 1.5 months. In two studies that did not

comply with GLP, in which groups of three rabbits were given

lincomycin, only the lowest dose of 0.5 mg/kg bw was not lethal. All

the other doses (5, 50, 100, and 150 mg/kg bw) caused death, such that

by 4 weeks 9 out of 15 and 12 out of 15 rabbits had died. Histological

examination revealed gastrointestinal stasis and, in those animals

that died, haemorrhagic suffusion of the serosal surface of the

caecum. Attempts to modify the toxicity by supplementation with

*Lactobacillus* culture or intubation with fresh (rabbit) caecal

contents were not successful. The observed toxicity was considered to

result from gastrointestinal Gram-positive floral imbalance.

The irritability of lincomycin to tissues was investigated in

rabbits in a series of studies that did not comply with GLP. Doses of

up to 300 mg/kg bw were injected into the lumbar muscle at pH 4 (Gray

& Purmalis, 1962b) or pH 7.4 (Gray & Purmalis, 1962c). No difference

was seen in the minimal to mild muscular irritation after slaughter up

to 7 days after treatment. Injection of up to 150 mg of lincomycin

into the stifle joint of New Zealand white rabbits caused no

treatment-related effects, such as intra-articular irritation (Gray &

Highstrete, 1965).

ADVERSE EFFECTS.

Leukopenia, agranulocytosis, neutropenia, thrombocytopenic purpura, hypotension, hypersensitivity reactions (serum sickness, angioneurotic edema, anaphylaxis), vomiting, abdominal distress, nausea, persistent diarrhea , abdominal liver function tests, vaginitis, urticaria, skin rashes, exfoliative and vesiculobullous dermatitis.