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Historical perspective: Trace the history of leprosy, including its prevalence, treatments, and social stigma over time.

Kusum, Chanchal Sahu, Miss Anjali
(Rungta Institutee Of Pharmaceutical Sciences And Research)
(Rungta Institutee Of Pharmaceutical Sciences And Research)

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ABSTRACT
Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by the bacteria Mycobacterium leprae. It primarily affects the skin, peripheral nerves, and mucous membranes, leading to disfiguring skin lesions and nerve damage. Leprosy is transmitted through close and prolonged contact with an infected person, but its exact mode of transmission is not fully understood. The disease has been present for centuries and carries significant social stigma due to its visible symptoms. Early diagnosis and treatment are crucial in preventing disability and further transmission. Multi-drug therapy (MDT) is the standard treatment for leprosy and involves a combination of antibiotics that kill the bacteria and reduce the risk of relapse.A comparison study between antileprotic drugs is important for determining the most effective treatment for individuals with leprosy. There are several antileprotic drugs available, including dapsone, rifampicin(RMP), and clofazimine(Cfz), and they vary in terms of efficacy,stability,contentuniformity,weight variation.

KEYWORDS-
MDT,LEPROSY,ANTIBIOTICS,RMP,Cfz.

ABBREVIATION-Cfz(clofazimine)
RMP(rifampicin)
MDT(multi-drug therapy)

I. INTRODUCTION

1.1 LEPROSY

Leprosy is a type of skin and neurological disease that affects the eyes,respiratorytract,and peripheral nerves[1]. The discovery of MYCOBACTERIUM LEPRAE by Gerhard Armauer Hansen in 1873 was the first time that bacterium was identified as the cause of this disease in humans is a long-lasting infectious disease that affects humans and is still a significant public health issue in many underdeveloped nations[2],[3]. M. leprae is an obligate intracellular pathogen that grows slowly and can live outside of its human host for up to 45 days, because of the patient's limitations and negative social repercussions [4], leprosy is a dangerous contagious disease that affects both the patient and the community [5].

Leprosy is a treatable illness that has been eradicated from numerous nations, including India. This has been made possible by the abundance of powerful and secure medications [6].

1.2 STRUCTURE

Leprae's mycobacterium Since it is an obligate intracellular parasite and an acid-fast, Gram-positive, rod-shaped bacterium, it cannot be cultured in cell-free laboratory media like its relative Mycobacterium tuberculosis [7],[8].

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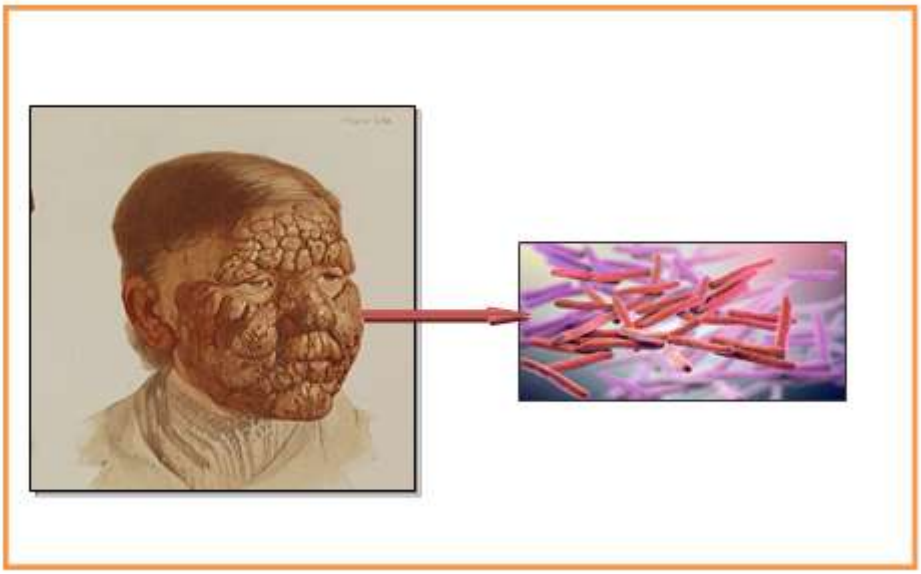
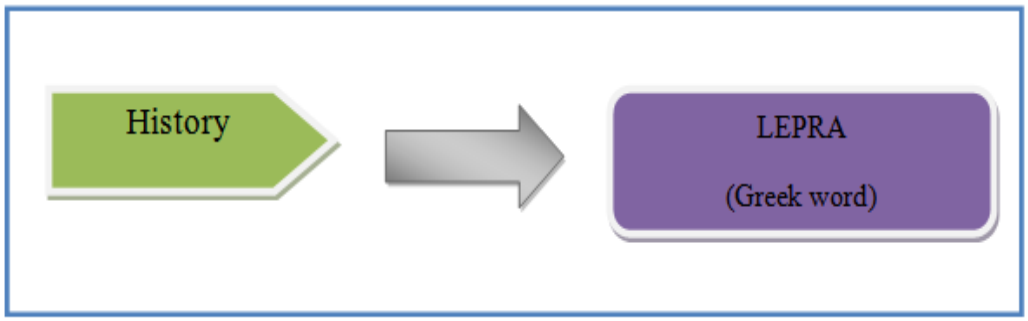


FIGURE 1 –MICOBACTERIUM LEPRAE

1.3 HISTORY



Lepra – Means "a disease that make the skin scaly" [9].

India has the unfortunate distinction of being the leprosy's original source. It is believed that the disease first spread to China[10], Egypt, and the Middle East through trade and conflict before moving on to Europe and the Americas[11]. Indian society has treated leprosy exclusively for tradition and law from antiquity to the present, a reaction molded by both scientific understanding and cultural views [12]. Eminent medical professionals and researchers in India have been working tirelessly for centuries to better understand the clinical, bacteriologic, pathologic, and immunologic aspects of leprosy[13],[24].

Indicated by skeletal evidence from the second century BCE, India may have been the origin of leprosy[15]. Intriguingly, Mycobacterium leprae may have developed in East Africa or South Asia during the Late Pleistocene epoch (11,700–129,000 years ago), according to comparative genomics studies[16]. It is believed that the disease spread to other regions of Asia, the Middle East, and across the continents of Africa, Europe, and the Americas through trade routes and ensuing battles [17].Leprosy has been mentioned for the first time in osteo-archaeological remains discovered in India and dating to 2000 BC[18],[19].The oldest leprosy evidence was found in a 4,000-year-old human skeleton that was discovered in India in 2009[20],[21].

The skeleton was discovered to show erosion patterns resembling those of leper skeletons from the Middle Ages in Europe exhibits damage to the peripheral skeleton, degenerative joint disease, infectious involvement of the tibia (periostitis), and pathological alterations in the rhinomaxillary[22],[23].

Skeletons provide practically all of the evidence for leprosy.

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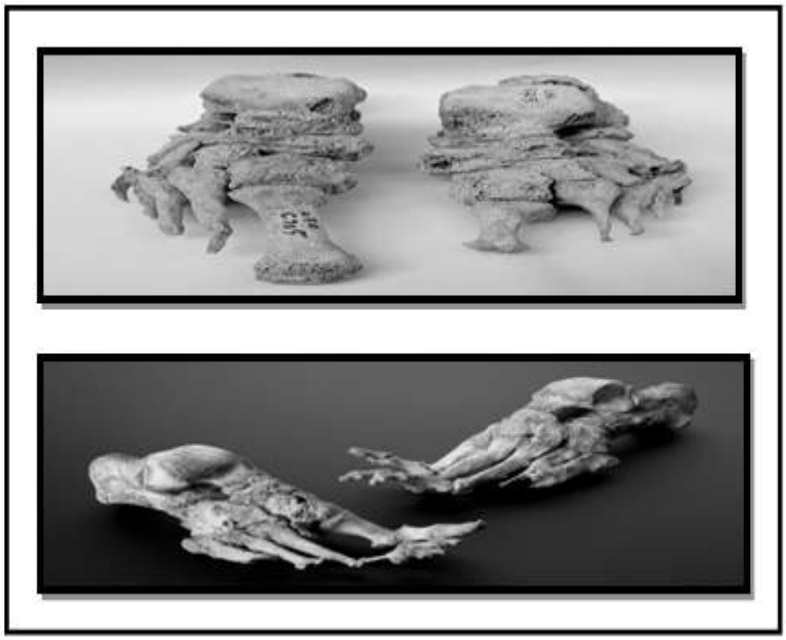

FIGURE 2-SKELETON EVIDENCE

II. EFFECTS OF LEPROSY

The peripheral nervous system (PNS), which consists of neurons and glial cells (Schwann cells) that build myelin sheaths around certain axons, connects the central nervous system to the rest of the body[24]. An intracellular bacterium called M. leprae invades the PNS's Schwann cells[25]

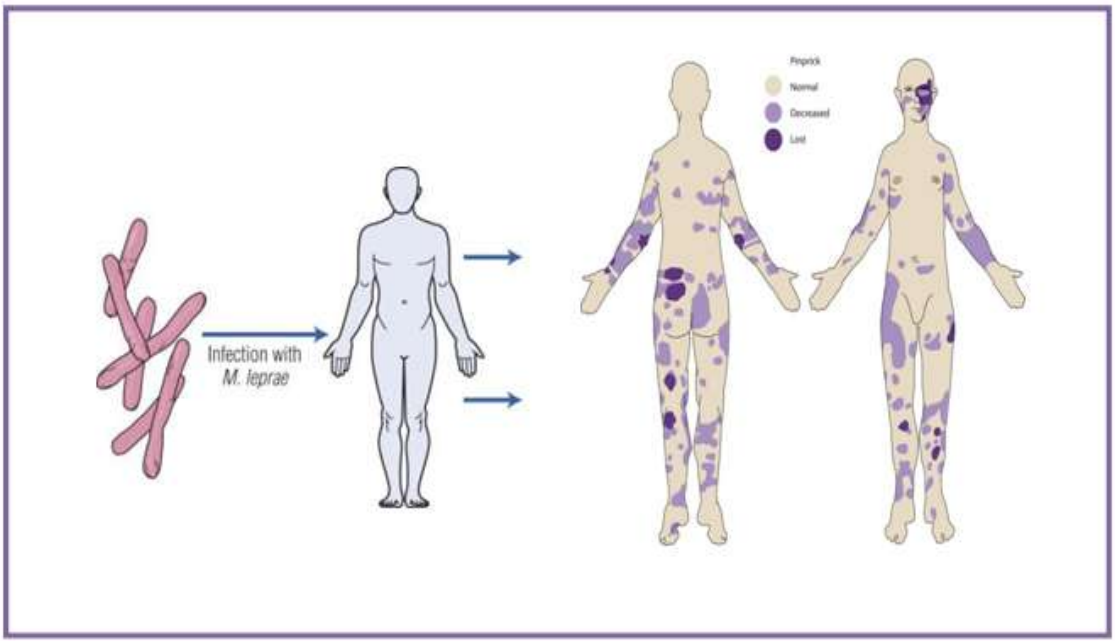

FIGURE3-EFFECT OF LEPROSY

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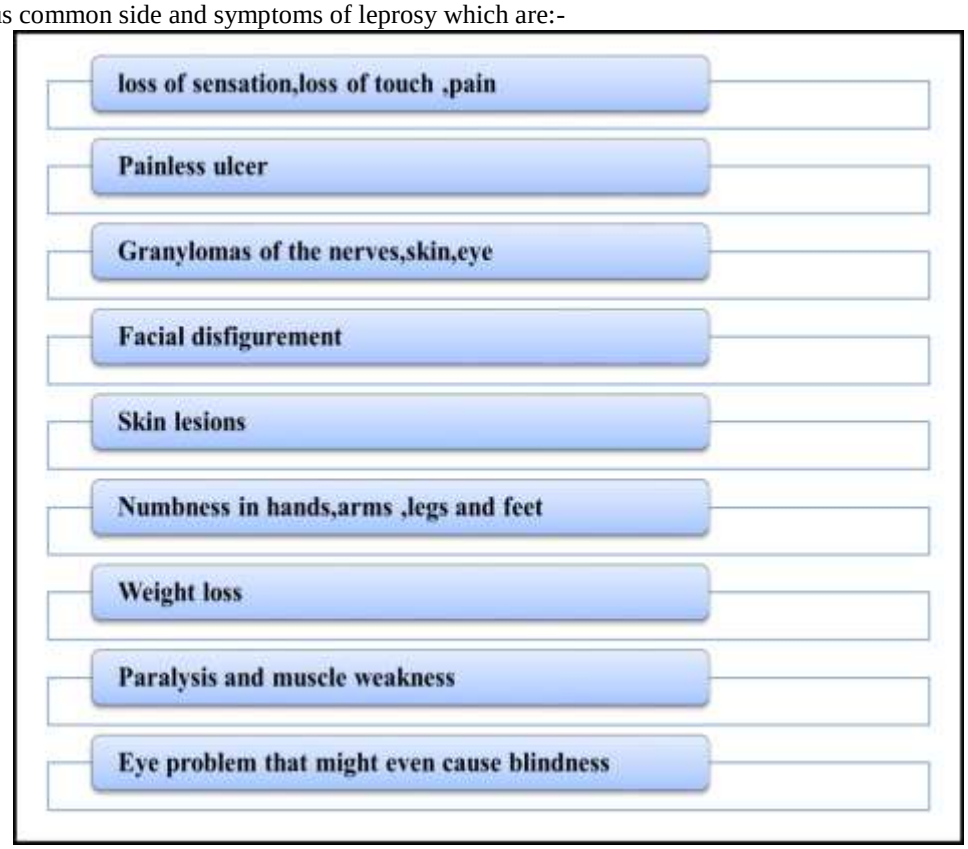
2.1SIGN AND SYMPYOMS

The various common side and symptoms of leprosy which are:-



2.2 TRANSMISSION

Droplets from the lips and nose are how the sickness is spread. Leprosy must be contracted through months of close, continuous contact with an untreated patient[26]. Leprosy cannot be contracted by simply shaking hands, hugging, eating together, or sitting near to someone who has the disease. In addition, once therapy starts, the patient stops spreading the illness[27].

Although the precise mode of M. leprae transmission is not fully understood, prolonged contact and crowding are known to be risk factors. Since a significant number of the bacteria were found in nasal mucosa, it has been hypothesized that the respiratory system may be involved in the transmission of M. leprae [28]. There have also been reports of disease transmission from mother to unbor n child during pregnancy, leading to cases of leprosy patients [29].

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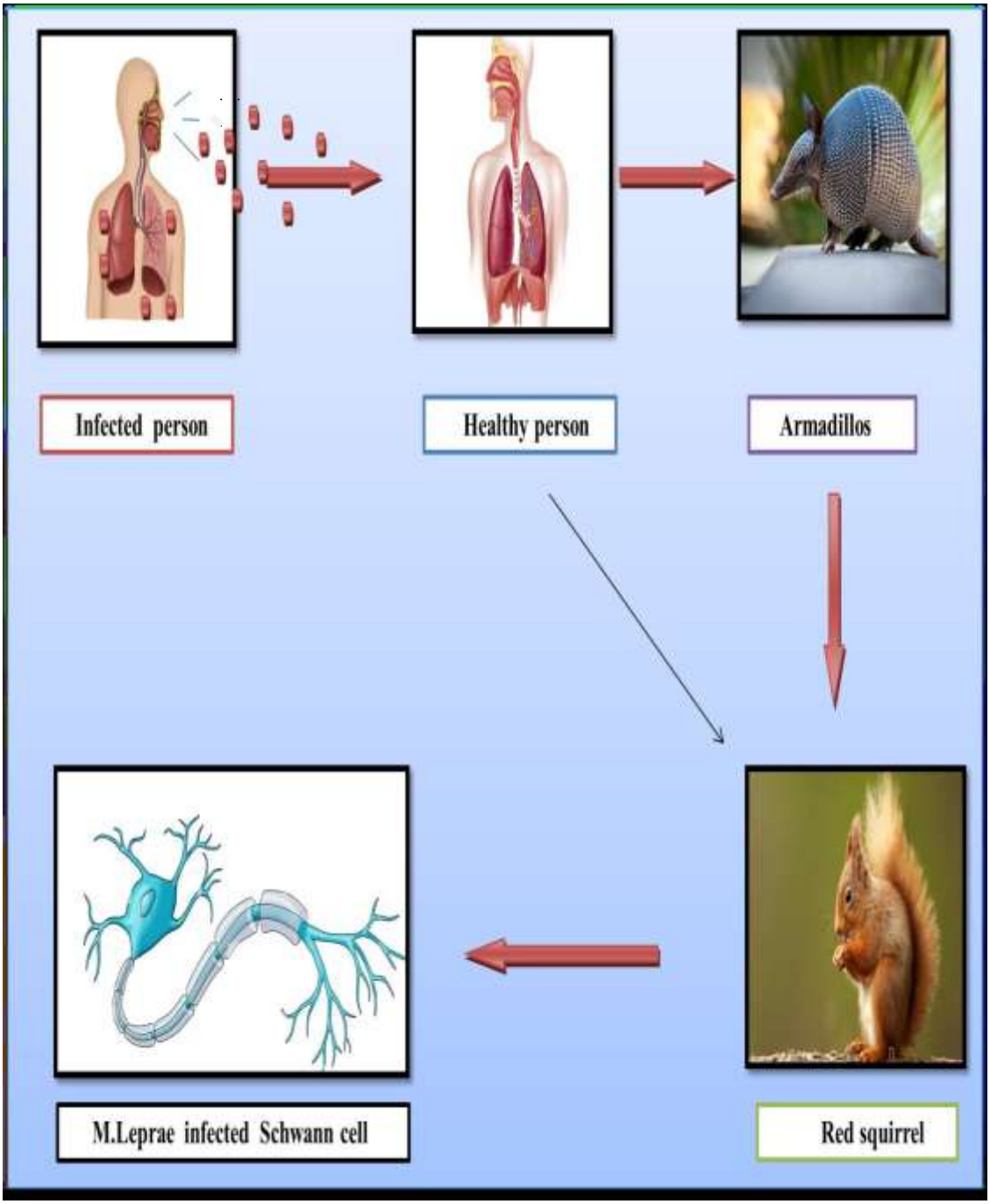

FIGURE 4-TRANSMISSION OF LEPROSY

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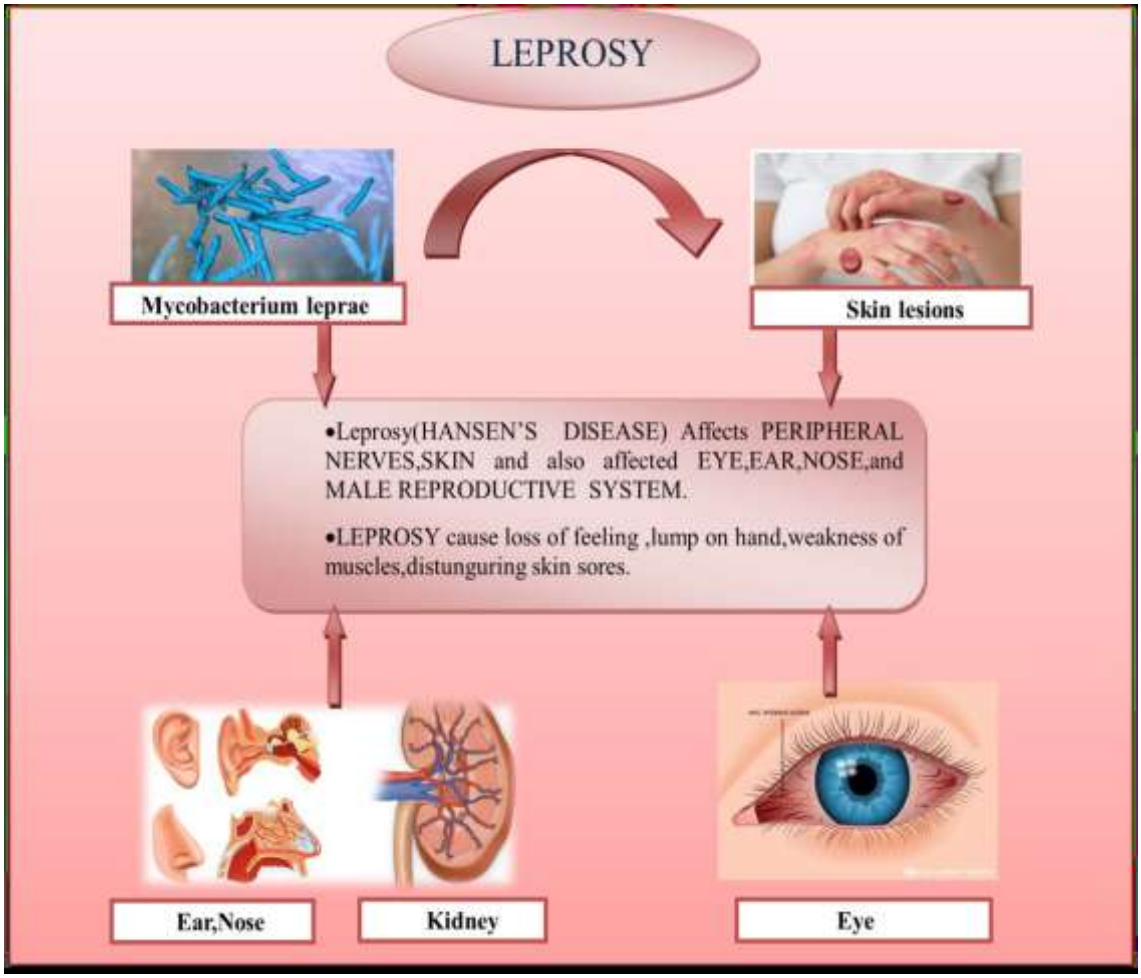
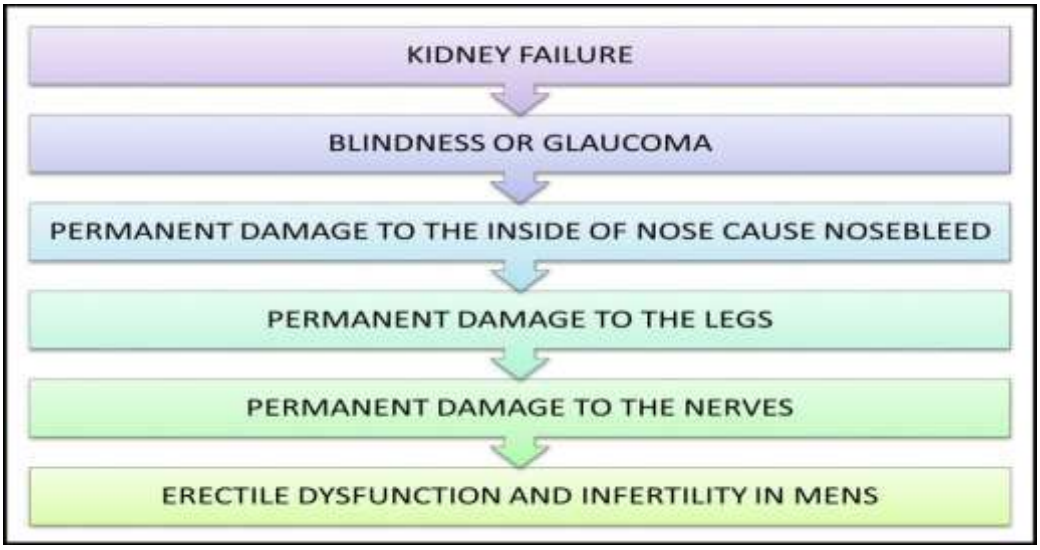


FIGURE 5-LEROTIC EFFECT'S

III. COMPLICATED LEPROSY



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IV. CLASSIFICATION

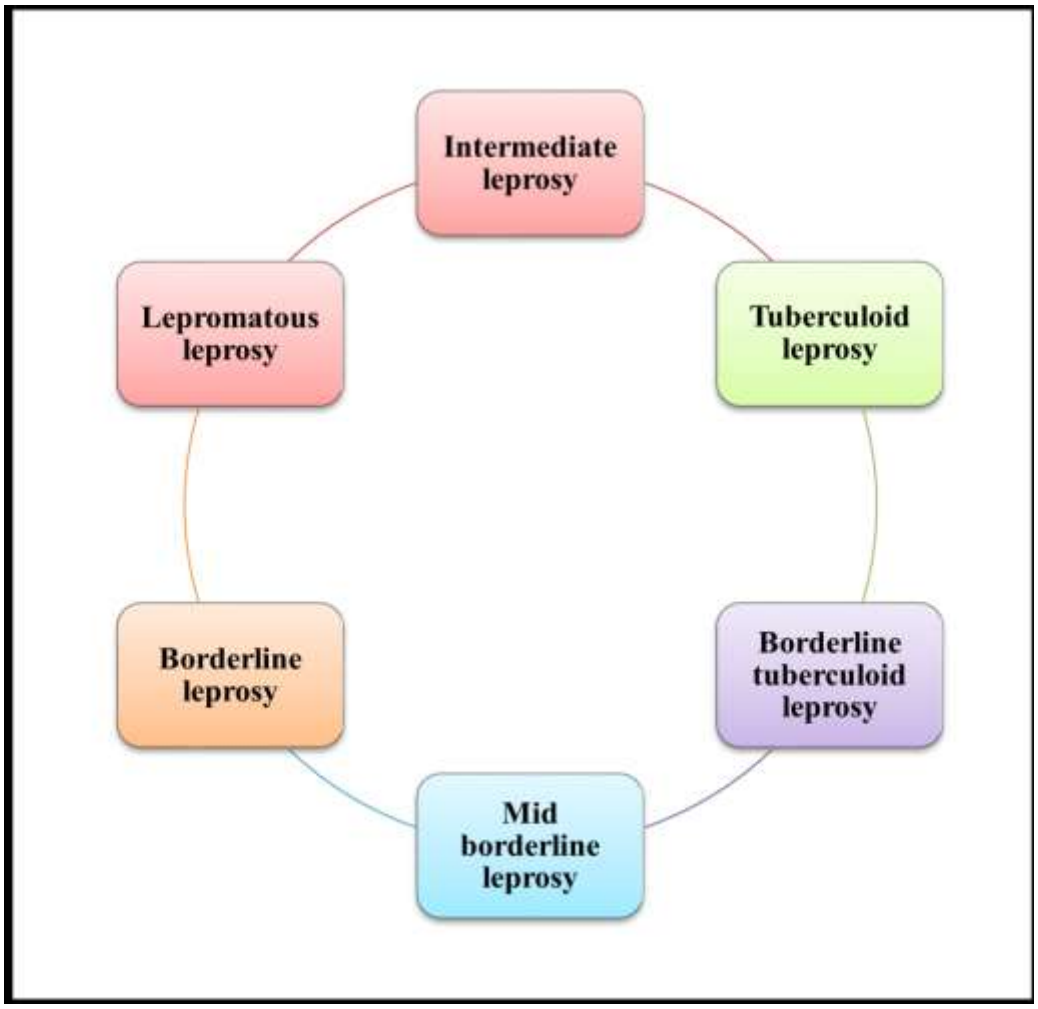

FIGURE 6-Classification of leprosy

The six different forms of leprosy—Intermediate, Tuberculoid, Borderline Tuberculoid, Mid-borderline, Borderline, and Lepromatous leprosy—are mostly categorized depending on the severity of the symptoms.

1.INTERMEDIATE LEPROSY

It is leprosy's initial stage. Patients in this stage have flat lesions that, in the event of a strong immune system, may heal on their own without advancing.

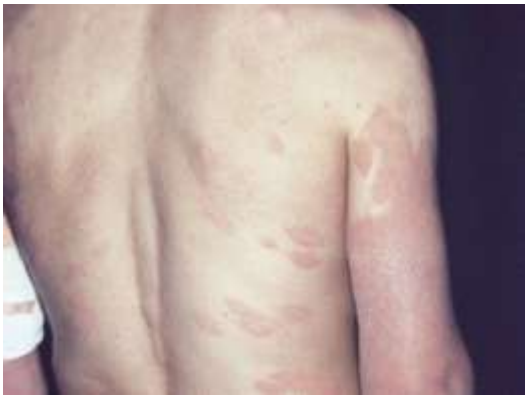

FIGURE 7-INTERMEDIATE LEPROSY

2.TUBERCULOID LEPROSY

It is a less severe and milder form of leprosy. Due to nerve loss, those who have this condition have some patches of flat, pale-colored

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skin and are numb in the affected area. Comparable to other kinds, this is less contagious. This infection either goes away on its own or it can linger and get worse.

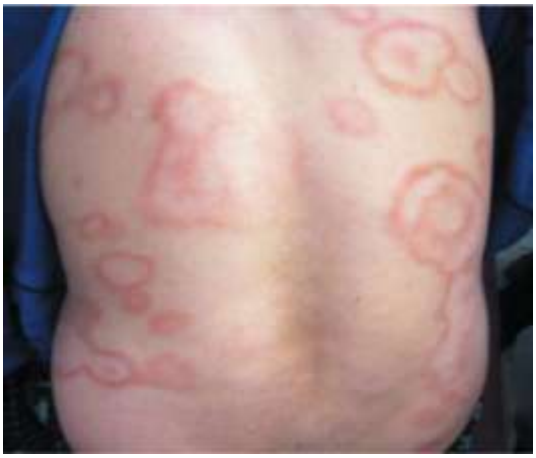

FIGURE 8-TUBERCULOID LEPROSY

3.BORDERLINE TUBERCULOID LEPROSY

Although the infections may be smaller and more numerous at this stage, they could still persist and revert to tuberculoid or any other advanced type. The symptoms at this stage are remarkably similar to those of tuberculoid.

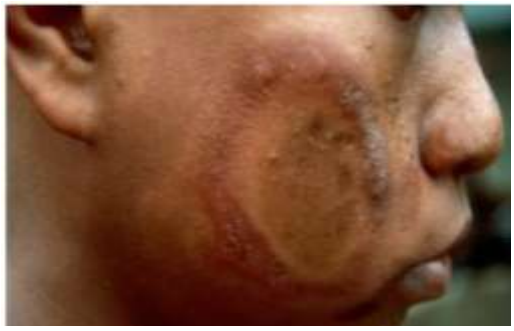

FIGURE 9 –BORDERLINE TUBERCULOID LEPROSY

4.MID BORDERLINE LEPROSY

This stage's signs and symptoms resemble those of borderline tuberculoid leprosy quite a bit. This contains numbing reddish plaques that could regress or change into another shape.

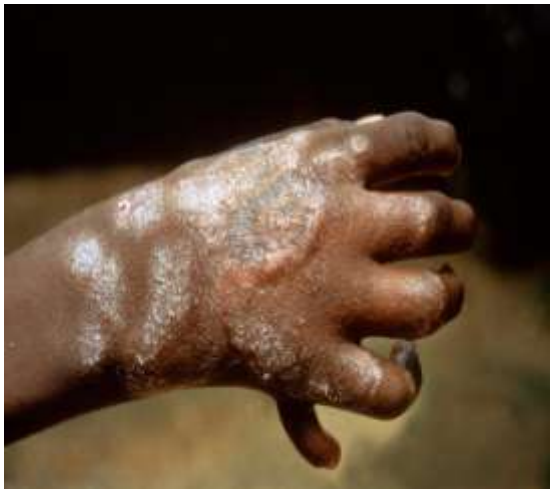

FIGURE 10 –MID BORFERLINE LEPROSY

5.BODERLINE LEPROSY

The primary signs of this type of leprosy, which is a cutaneous skin ailment, are numerous wounds or scars, including plaques, and flat, raised lumps that may persist or regress.

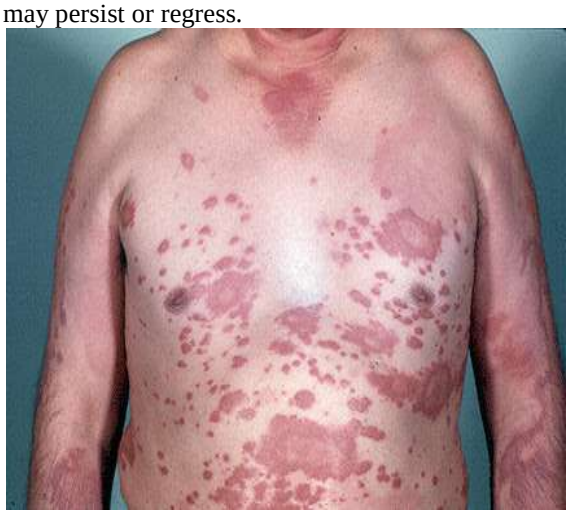

FIGURE 11-BORDERLINE LEPROSY

6.LEPROMATOUS LEPROSY

It is regarded as a more severe type of sickness since it causes numerous bacterial lesions. There are numerous pimples, rashes, numbness, and muscle weakness in the affected area. Other signs include hair loss, limb weakness, and damage to the male reproductive system, nose, kidneys, and other body organs. Compared to tuberculoid leprosy, which never improves, it is more contagious.

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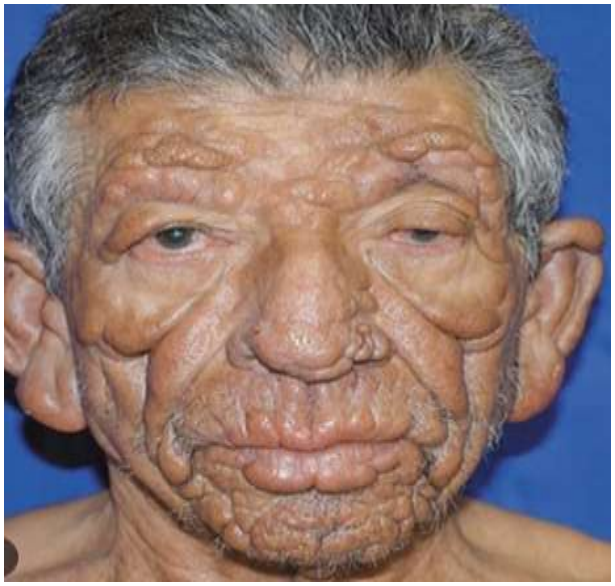

FIGURE 12-LEPROMATOUS LEPROSY

V. ANTI-LEPROTIC DRUGS

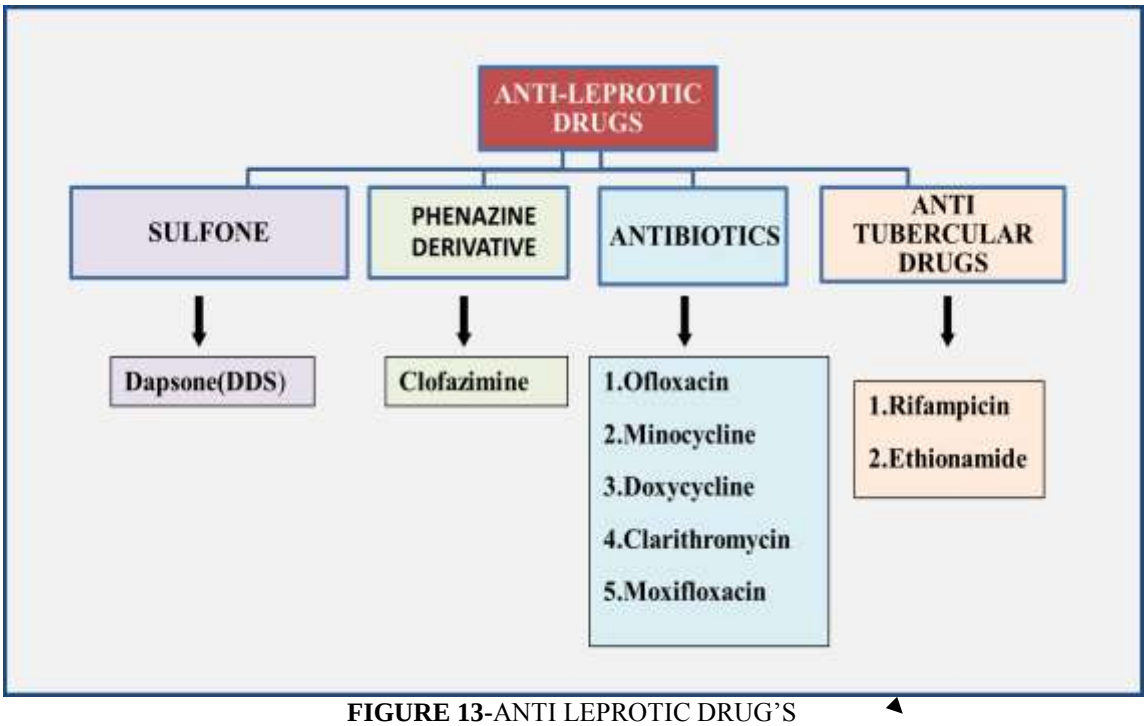

FIGURE 13-ANTI LEPROTIC DRUG'S

5.1DAPSONE

Dapsone was the first anti leprotic durg it is the first line drug of leprosy.

Dapsone is a bacteriostatic medication that works by competitively inhibiting dihydrofolate synthetase and dihydrofolate reductase, two important enzymes in M. leprae's pathway for making folate [31].5 Dapsone monotherapy patients experienced total bacilli killing in 3 to 6 months, although complete clinical regression typically takes 2 to 3 years [32]. As with all antileprosy medications, mucosal lesions heal first and are followed by skin ulcers, clearing the nasal passages, subsiding epistaxis, and a reduction in foul-smelling nasal discharge. Regression of nodules and skin thickening begins later [33].

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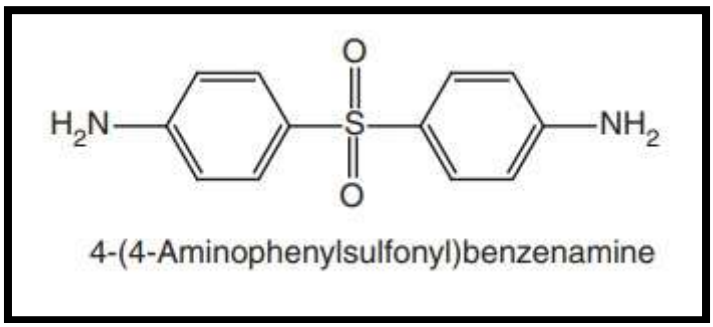
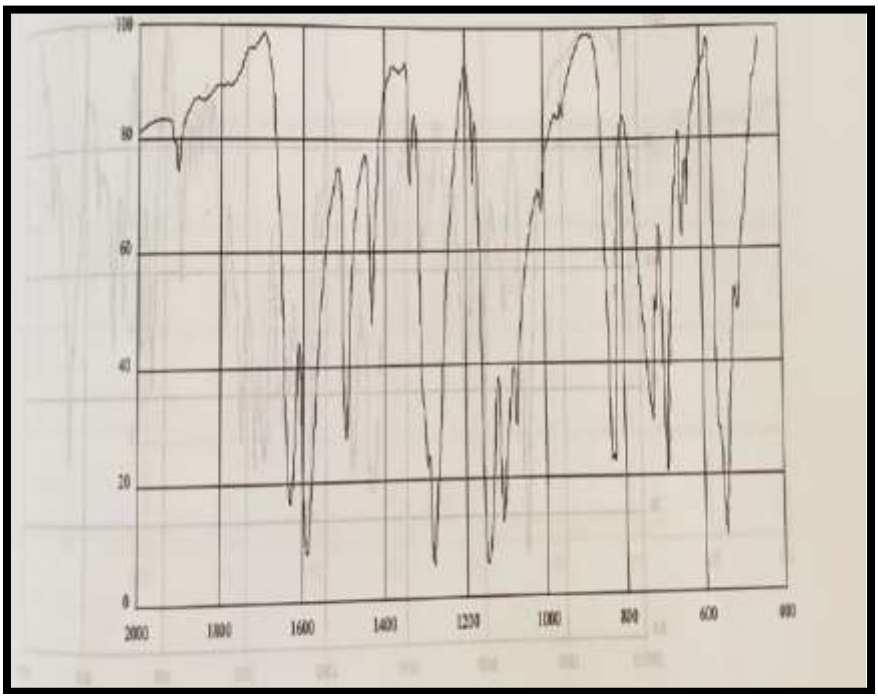
Response times for trophic ulcers, sensorimotor loss, and nerve thickening are incredibly long and frequently fall short. Special attention and protection from burns and injury are required for the eyes and extremities.5 Dapsone does have certain well-known side effects, despite being well-tolerated[34].



STRUCTURE-1 DAPSONE



FTIR-1 DAPSONE

5.2CLOFAZIMINE

Brick-red, fat-soluble crystalline dye clofazimine has bacteriostatic and anti-inflammatory properties; its biochemical basis for antibacterial properties is still unknown. The medicine may exert its effects by preventing DNA from serving as a template, boosting the production of lysosomal enzymes, and improving macrophage phagocytic capacity.7 It preferentially attaches to mycobacterial DNA, not mammalian DNA, that has a lot of GC (guanine-cytosine).Through the promotion of prostaglandin E2 (PGE2) synthesis, inhibition of neutrophil motility, and selective reduction of Th1 subtype of T helper cells, it has anti-inflammatory properties and is useful in treating type 2 leprosy responses (T2R)[35].

8 Nuclear factors of activated T cells (NFAT) and nuclear factor-B (NFB) promote the synthesis of interleukin 2 (IL-2), a key cytokine in type 1 leprosy reactions (T1R), which produce neuritis. By disrupting the oscillation frequency of the calcium-release activated calcium channel and blocking only the Kv1.3 potassium channel, clofazimine selectively inhibits the calcineurin-NFAT signaling pathway.All recommended MDT regimens primarily consist of rifampicin (3-[(4-

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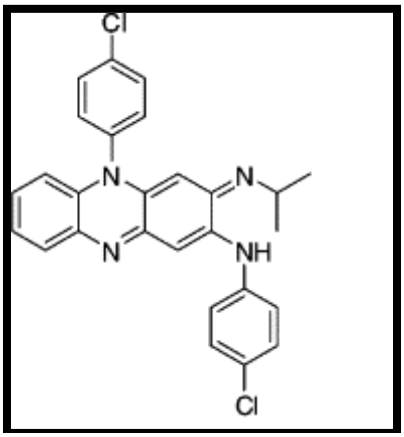
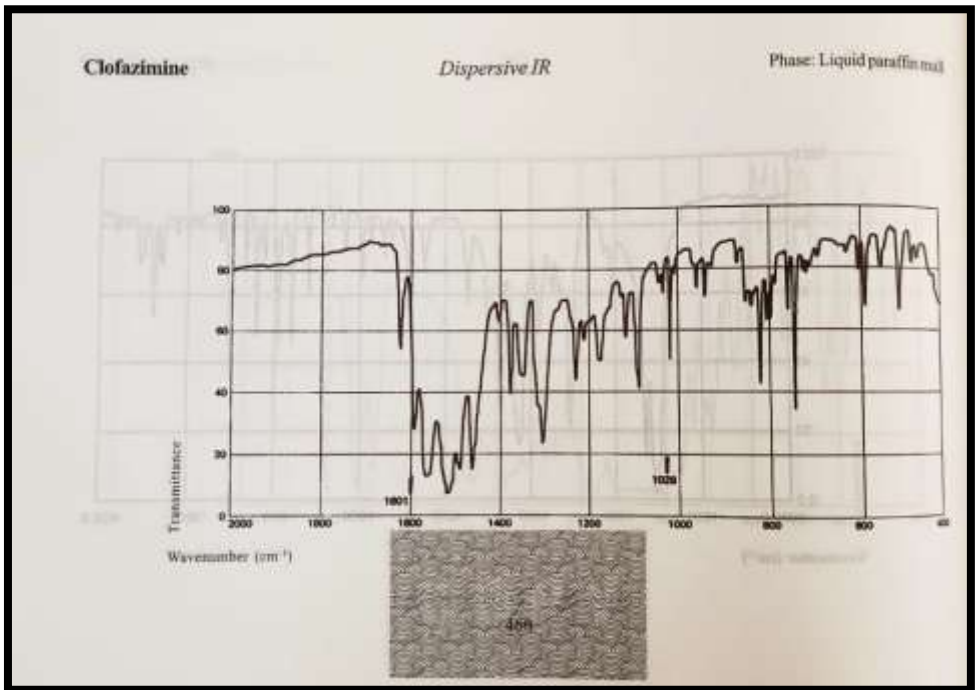
methyl-1-piperazinyl)-imino]-methylrifamycin), which is the primary bactericidal agent. Within a few days, a single 1,200 mg dose can cause the quantity of live bacteria in a patient's skin to drop to undetectable levels.32 A single 600 mg dose had the same effect as 1200 mg in roughly 7 days, according to one study. The b-subunit of the rpoB-encoded DNA-dependent RNA polymerase is the target of rifampicin in bacteria [36].



STRUCTURE-2 CLOFAZIMINE



FTIR-2 CLOFAZIMINE

5.3RIFAMPICIN

The rifampicin resistance determination region (RRDR), a highly conserved area of the rpoB gene, is responsible for determining rifampicin resistance in M. tuberculosis, and changes in this region are correlated with changes in the structure of the b-subunit of RNA polymerase.6,41 Additionally, missense mutations in the rpoB RRDR are correlated with rifampicin resistance in M. leprae [35], [37].

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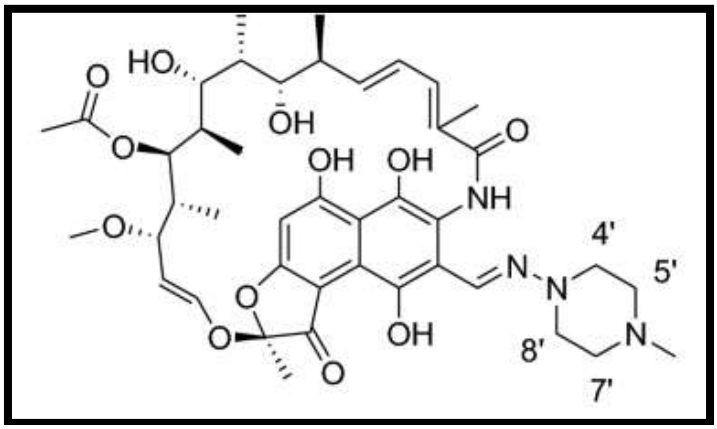
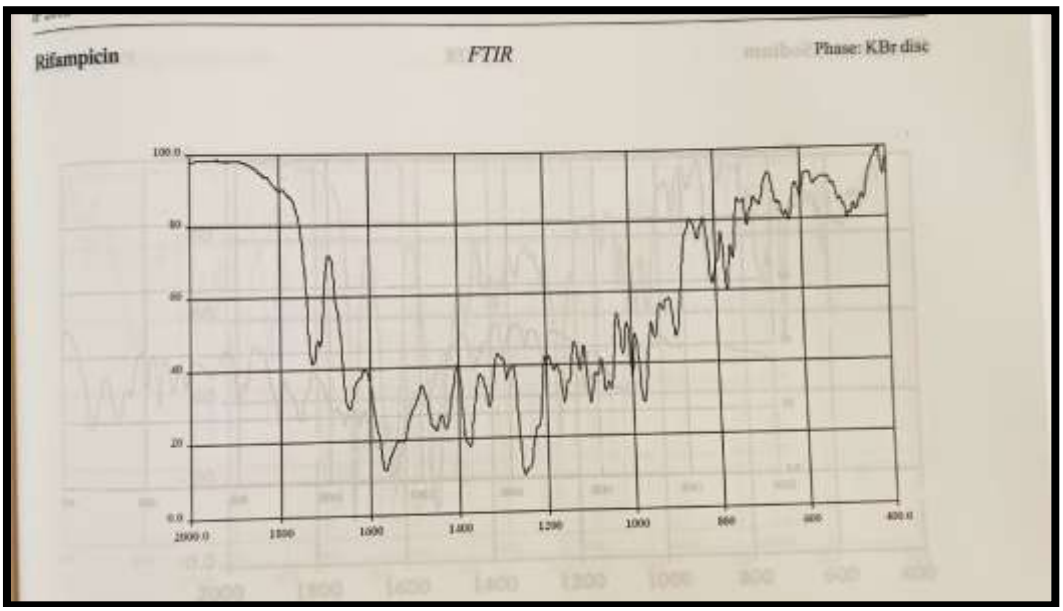


STRUCTURE-3 RIFAMPICIN



FTIR-3 RIFAMPICIN

5.4CLARITHROMYCIN

The semi-synthetic macrolide clarithromycin varies from erythromycin by having a methyl substitution at the macrolide ring's position six [38].

Significant bactericidal efficacy against M. leprae in humans is demonstrated by this medication.Significant bactericidal efficacy against M. leprae in humans is demonstrated by this medication [39].

A daily dose of 500 mg of clarithromycin eliminates 99.9% of live M. leprae in lepromatous leprosy patients after 28 days and 99.9% after 56 days . Despite the fact that the exact method of action against M. leprae is unknown, it is believed to be comparable to erythromycin, which inhibits protein synthesis by binding to the ribosome [40].

Clarithromycin resistance in bacteria and mycobacteria appears to be brought on by a reduction in the drug's ability to bind to ribosomes and is linked to missense mutations [41].

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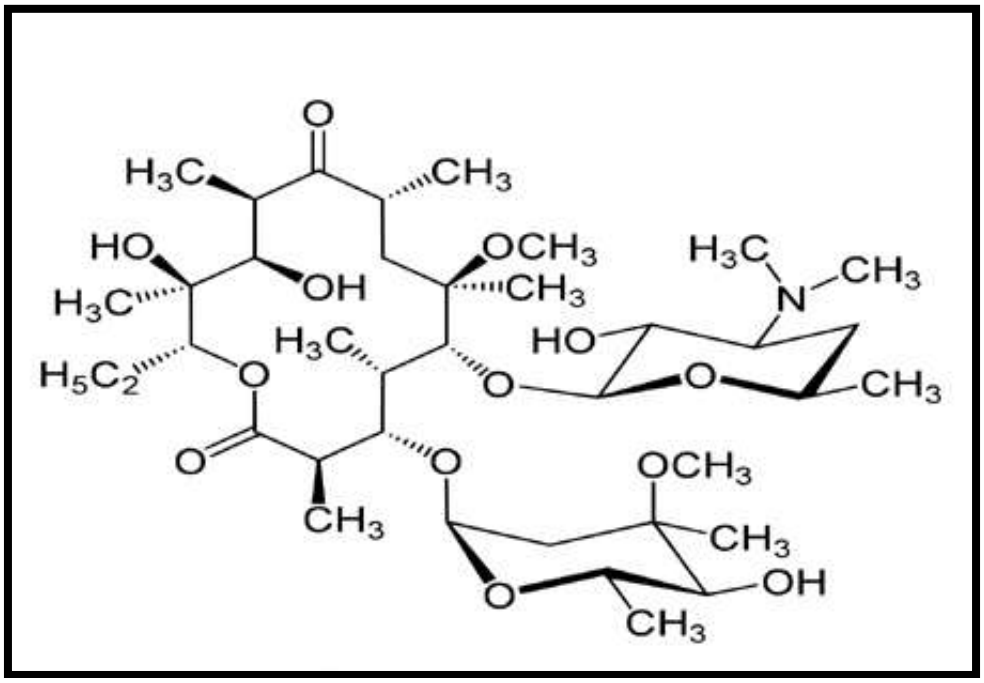
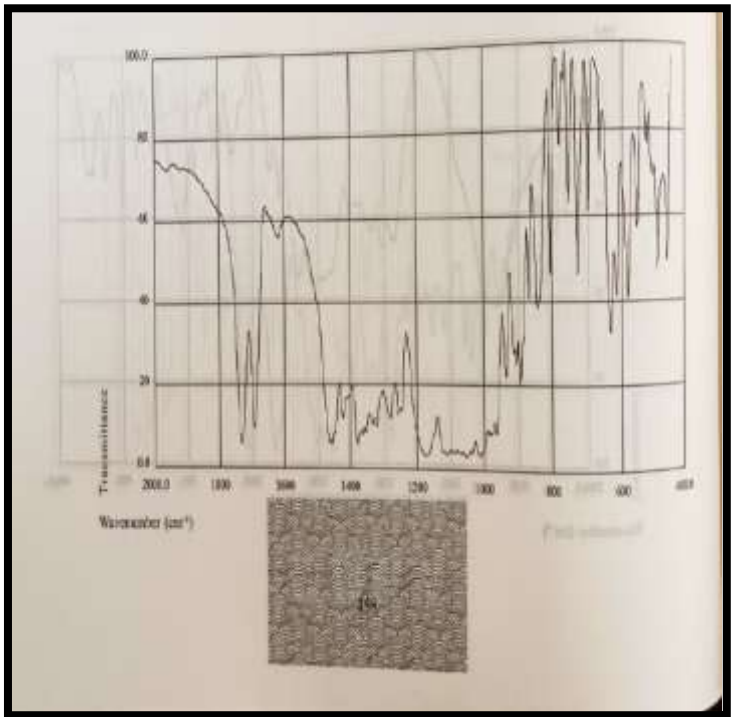


STRUCTURE-4 CLARITHROMYCIN



FTIR-4CLARITHROMYCIN

5.5DOXYCYCLINE

Doxycycline is an antibiotic that is commonly used in the treatment of various bacterial infections, including leprosy.

Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by the bacteria Mycobacterium leprae.

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Doxycycline is part of the multidrug therapy (MDT) regimen recommended by the World Health Organization (WHO) for the treatment of leprosy. MDT is a combination therapy that includes doxycycline along with other antibiotics such as rifampicin and clofazimine [42].

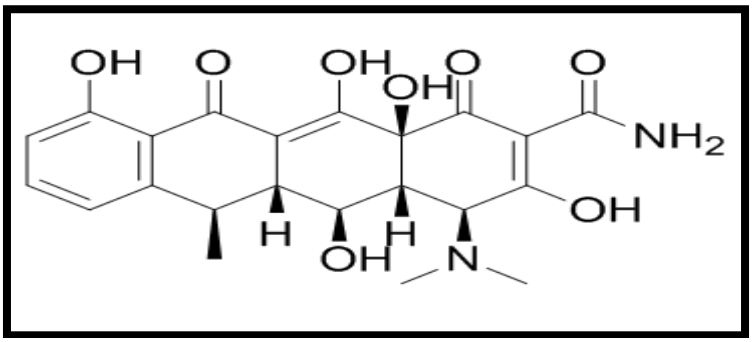
The role of doxycycline in the treatment of leprosy is primarily as a bacteriostatic agent, meaning it inhibits the growth and replication of the bacteria rather than killing them outright. It works by interfering with the protein synthesis process in the bacteria, thereby preventing their multiplication.

Doxycycline is particularly effective against leprosy because it has good tissue penetration and can reach high concentrations in skin and other affected tissues [43]. It is also active against both actively dividing and dormant forms of the bacteria, making it useful in treating both early and late-stage leprosy.

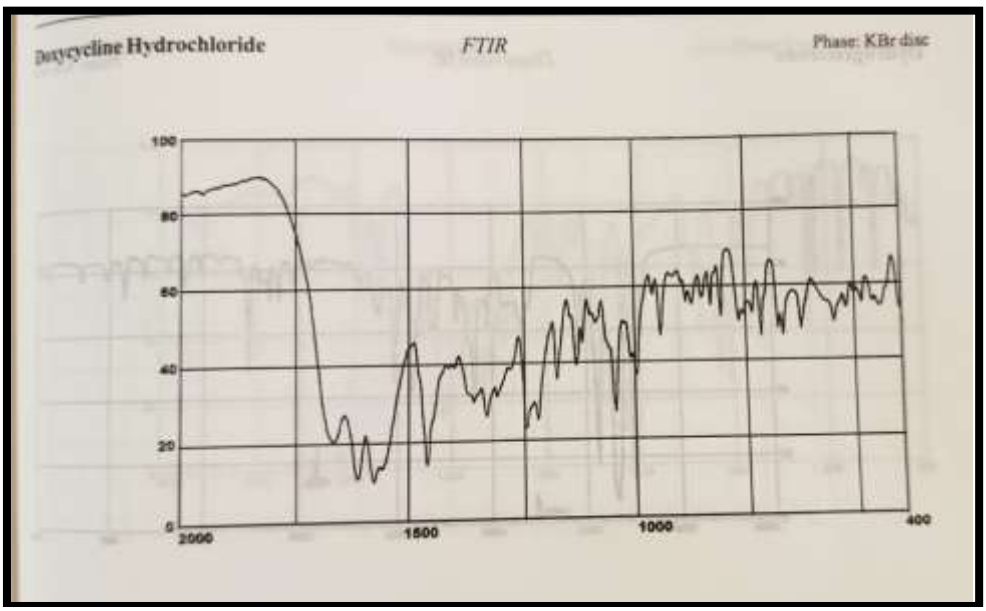
In addition to its direct antibacterial effects, doxycycline has been found to have immunomodulatory properties. It can help modulate the immune response and reduce the inflammatory reactions associated with leprosy, leading to improved clinical outcomes [44].

It is important to note that doxycycline should always be used in combination with other antibiotics as part of a comprehensive treatment plan for leprosy. The specific dosage and duration of treatment will depend on the severity and stage of the disease, as well as individual patient factors [45].

Overall, doxycycline plays a crucial role in the treatment of leprosy by effectively inhibiting bacterial growth and reducing inflammation, leading to improved clinical outcomes for patients.



STRUCTURE-5 DOXYCYCLINE



FTIR-5 DOXYCYCLINE

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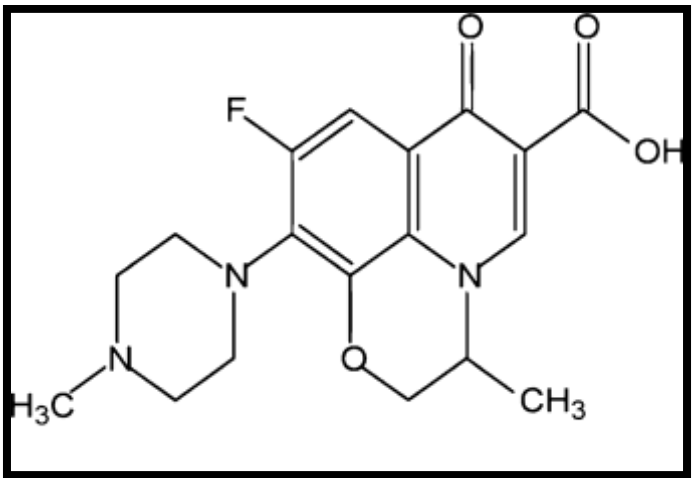
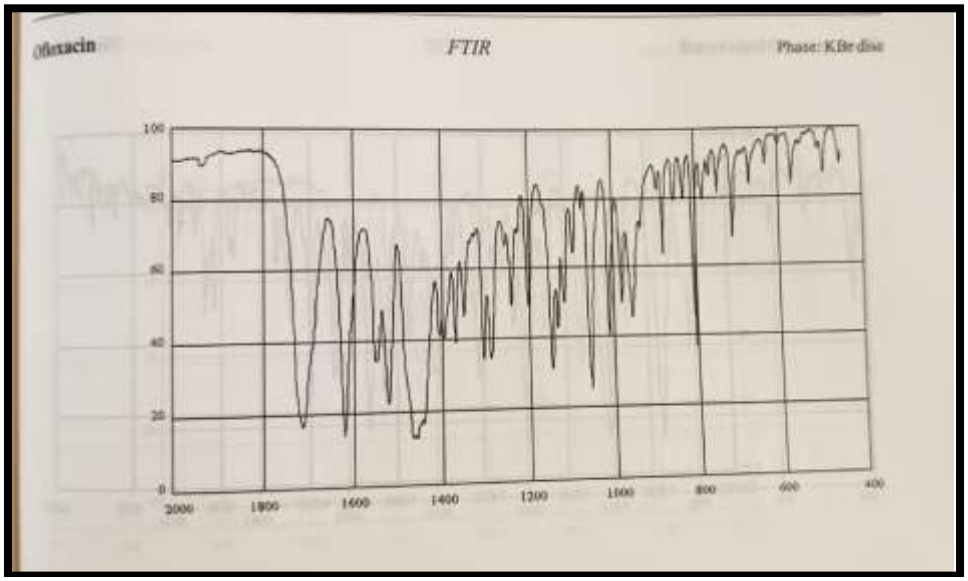
5.6OFLOXACIN

Ofloxacin is another antibiotic that can play a role in the treatment of leprosy. It belongs to the fluoroquinolone class of drugs and is effective against various bacteria, including Mycobacterium leprae [46].Similar to minocycline, ofloxacin is included in the multidrug therapy (MDT) recommended by the World Health Organization (WHO) for leprosy treatment. It is often used in combination with other antibiotics to target the bacteria and prevent drug resistance [47] [48].

Studies have shown that ofloxacin has good bactericidal activity against M. leprae and can effectively reduce the bacterial load in leprosy patients . It is particularly useful in cases where other drugs like dapsone or rifampicin cannot be used due to contraindications or drug resistance [49].In addition to its antibacterial properties, ofloxacin also has anti-inflammatory effects. This can help reduce the inflammation caused by leprosy and potentially prevent further nerve damage [50].



STRUCTURE-6 OFLOXACIN



FTIR-6 OFLOXACIN

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VI. CONCLUSION

The most effective leprosy treatment is WHO-MDT(multiple drug therapy).

There is enough data to support further investigation of various newer treatment regimens containing one of the FQs on a much larger scale with the goal of incorporating them into the National Leprosy Eradication Program. Newer medications, particularly fluoroquinolones, have also demonstrated excellent efficacy against M leprae. Despite the availability of MDT therapy, leprosy is still a widespread illness. To solve the issues of medication resistance and drug-related adverse effects, alternative medicines must be created. To address the current gaps in disease diagnosis, treatment, management, and care, new interventions are needed. To develop therapies like novel vaccines for disease prevention and management, there needs to be an acceleration of study into the biology of the pathogen and the characteristics of the host's cellular immune response.

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