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Review Article

PHARMACOKINETIC, SOLUBILITY AND DISSOLUTION PROFILE OF LEPROTIC DRUGS.

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Abstract
Pharmacokinetic data And Solubility Profile Of drugs are the basic requirement of any researcher, for selecting an appropriate drug for any kind of formulation development. To get such data of all drugs of any category at one place is very difficult task; we by our review article have tried to give all such data of Leprotic drugs at one place.

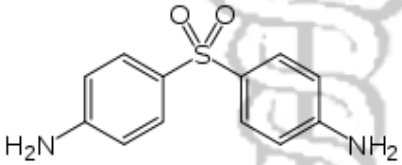
Keywords: - Solubility profile, pharmacokinetic parameters.Leprosy.

Introduction

Classification: - [1]

1. **Sulphones:** - Dapsone,Sulfoxone sodium.
2. **Non-Sulphones:** - Rifampin,Clofazimine,Thiacetazone,Sulfadoxine,Asprin,Chloroquine,Thalidomide,Antimonials,Corticosteroids.

Dapsone [2]



Systematic (IUPAC) name 4-[(4-aminobenzene)sulfonyl]aniline**[2]**

Chemical data

Formula: - $C_{12}H_{12}N_2O_2S$

Mol. Mass: - 248.302 $gmol^{-1}$

Melting point: - 175 - 176° C **[3]**

Description: - Dapsone is a white or slightly yellowish-white, odorless, crystalline powder with a slightly Bitter taste. **[3]**

Solubility profile: - Very slightly soluble in water, freely soluble in alcohol, soluble in acetone and in dilute mineral acid. **[USP][4]**

Solubility profile: -Freely soluble in ethanol (95 percent) and in acetone. Very slightly soluble in water. It is soluble in dilute mineral acid. **[IP][5]**

Pharmacology: -

Mechanism of Action: - Dapsone acts against bacteria and protozoa in the same way as sulphonamides, that is by inhibiting the synthesis of dihydrofolic acid through competition with Para-amino-benzoate for the active site of dihydropteroate synthetase. The anti-inflammatory action of the drug is unrelated to its antibacterial action and is still not fully understood.**[7]**

Pharmaceutics: -

Pharmacokinetic data: -

Bioavailability: - 70 to 80%

Protein binding: - 70 to 90%

Metabolism: - Hepatic (mostly CYP2E1-mediated)

Half-life : - 20 to 30 hours

Excretion: -Renal **[2]**

Nature: - Lipophillic. **[6]**

Log P: - 0.97**[6]**

PKa/Isoelectric Point: - 2.41**[7]**

Dissolution:- Dapsone Tablet

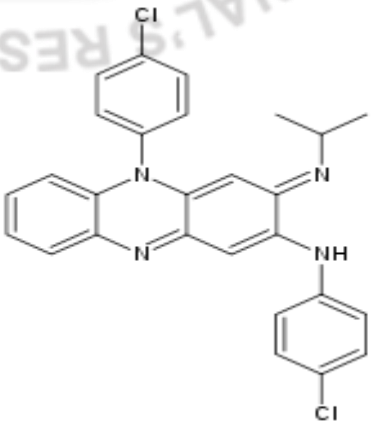
Medium: - Dilute hydrochloric acid(2 in 100),1000ml

Apparatus: - 1[USP]

Rpm: - 100 rpm

Time: - 60 minutes.**[8]**

Clofazimine [9]



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Systematic (IUPAC) name: - N, 5-*bis* (4-chlorophenyl)-3-(propan-2-ylimino)-3,5-dihydrophenazin-2-amine

Chemical data

Formula: - $C_{27}H_{22}Cl_2N_4$

Mol. mass: - 473.396 g/mol **[9]**

Melting point: - 210- 212 °C **[10]**

Description: -Dark red crystals. **[USP][11]**

Solubility profile: - Melt at about 217°, with decomposition. Practically insoluble in water, soluble in chloroform and in benzene. Sparingly soluble in alcohol, in acetone and in ethyl acetate.**[USP][11]**

Solubility profile: -Soluble in chloroform, in dioxane and in dimethylformamide, slightly soluble in ethanol (95 percent). Very slightly soluble in ether, insoluble in water.**[IP][12]**

Pharmacology: -

Mechanism of Action: - Appears to preferentially bind to mycobacterial DNA leading to disruption of the cell cycle and eventually kills the bacterium. It may also bind to bacterial potassium transporters, thereby inhibiting their function. Lysophospholipids have been found to mediate the activity of this drug.**[13]**

Pharmaceutics: -

Pharmacokinetic data: -

Absorption: - 45 to 62% after oral administration **[14]**

Half-life 70 days **[9]**

Distribution: - principally to fatty tissue and cells of the Reticuloendothelial system **[14]**

Elimination: - faeces and biliary **[14]**

Bioavailability: - 3.4.4**[14]**

Nature: - Lipophillic **[14]**

PKa/Isoelectric Point: - 8.51.**[13]**

Log P: - 0.3**[15]**

Dissolution: - Clofazimine capsule[16]

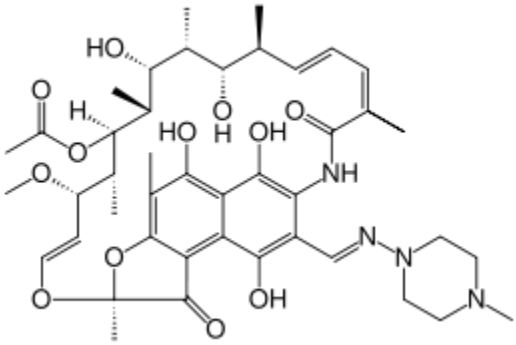
Medium: - water [500ml]

Apparatus: - 2[USP]

Rpm: - 50

Time: - 15 minutes.

Rifampin [17]



Systematic (IUPAC) name: - (7*S*,9*E*,11*S*,12*R*,13*S*,14*R*,15*R*,16*R*,17*S*,18*S*,19*E*,21*Z*)-2,15,17,27,29-pentahydroxy-11-methoxy-3,7,12,14,16,18,22-heptamethyl-26-{(E)-[(4-methylpiperazin-1-yl)imino]methyl}-6,23-dioxo-8,30-dioxa-24-azatetracyclo[23.3.1.1^{4,7}.0^{5,28}]triaconta-1(28),2,4,9,19,21,25(29),26-octaen-13-yl acetate

Chemical data

Formula: - $C_{43}H_{58}N_4O_{12}$

Mol. Mass: - 822.94 g/mol

Description: -Red brown, crystalline powder.**[USP][18]**

Solubility profile: -Very slightly soluble in water, freely soluble in chloroform, soluble in ethyl acetate and in methanol.**[USP][18]**

Solubility profile: -Soluble in chloroform and in methanol, slightly soluble in acetone, in ethanol(95 percent), in ether and in water. **[IP][19]**

Melt. Point: - 183–188 °C (361–370 °F)

Pharmacology: -

Mechanism of Action: -Rifampin acts via the inhibition of DNA-dependent RNA polymerase, leading to a suppression of RNA synthesis and cell death. **[21]**

Pharmacokinetic data

Bioavailability: - 90 to 95%

Metabolism: -Hepatic and intestinal wall

Half-life: -6 to 7 hours

Excretion: - 15 to 30% renal

Protein Binding: -89% **[21]**

*pKa***: -** 1.7 related to 4-hydroxy and 7.9 related to 3-piperazine nitrogen**[20]**

Log P: - 2.7**[21]**

Dissolution:-Rifampin Capsule [22]

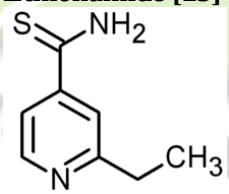
Medium: - 0.1N Hydrochloric acid [900 ml]

Apparatus: - 1

Rpm: - 100

Time: - 45

Ethionamide [23]



Systematic (IUPAC) name: - 2-ethylpyridine-4-carbothioamide

Chemical data

Formula $C_8H_{10}N_2S$

Mol. mass 166.244 g/mol

Melting Point: - 163 oC **[26]**

Description: - Bright yellow powder, having a faint to moderate sulfide-like odor. **[USP][24]**

Solubility profile: -Slightly soluble in water, in chloroform and in ether, soluble in methanol, sparingly soluble in alcohol and in propylene glycol. **[USP][24]**

Solubility profile: -Soluble in methanol, sparingly soluble in ethanol (95 percent), slightly soluble in chloroform and

in ether. Practically insoluble in water.**[IP][25]**

Pharmacology: -

Mechanism of Action: - Ethionamide may be bacteriostatic or bactericidal in action, depending on the concentration of the drug attained at the site of infection and the susceptibility of the infecting organism. Ethionamide, like prothionamide and pyrazinamide, is a nicotinic acid derivative related to isoniazid. It is thought that ethionamide undergoes intracellular modification and acts in a similar fashion to isoniazid. Isoniazid inhibits the synthesis of mycoloic acids, an essential component of the bacterial cell wall. Specifically isoniazid inhibits InhA, the enoyl reductase from *Mycobacterium tuberculosis*, by forming a covalent adduct with the NAD cofactor. It is the INH-NAD adduct that acts as a slow, tight-binding competitive inhibitor of InhA.**[26]**

Pharmacokinetic data: -

Protein binding: - Approximately 30% bound to proteins.

Half-life: - 2 to 3 hours

LogP: - 1.88**[26]**

Logs: --2.30**[26]**

pH: - 6.0 to 7.0 in a 1 in 100 slurry in Water. **[27]**

PKa/Isoelectric Point: -1.82**[26]**

Dissolution:-Ethionamide Tablet [28]

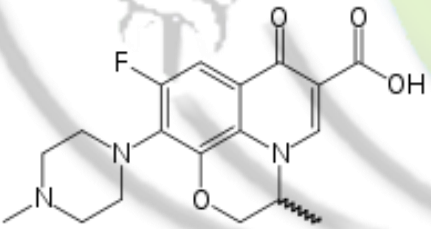
Medium: - 0.1N Hydrochloric acid [900 ml]

Apparatus: - 1

Rpm: - 100

Time: - 45

Ofloxacin [29]



Systematic (IUPAC) name: - (*RS*)-7-fluoro-2-methyl-6-(4-methylpiperazin-1-yl)-10-oxo-4-oxa-1-azatricyclo[7.3.1.$0^{5,13}$]trideca-5(13),6,8,11-tetraene-11-carboxylic acid.

Chemical data

Formula: - $C_{18}H_{20}FN_3O_4$

Mol. mass: -361.368 g/mol

Description: -Pale yellowish white to light yellowish-white crystals or crystalline powder. **[USP][30]**

Solubility profile: -Slightly soluble in alcohol, in methanol and in water. Sparingly soluble in chloroform. **[USP] [30]**

Solubility profile: -Soluble in glacial acetic acid, slightly soluble in water, methylene chloride and methanol. **[IP][31]**

Melting Point: - 250-257 oC **[32]**

Pharmacology: -

Mechanism of Action: - Ofloxacin acts on DNA gyrase, an enzyme which, like human topoisomerase, prevents the excessive supercoiling of DNA during replication or transcription. **[32]**

Pharmacokinetic data: -

Protein binding: - 32%

Half-life: - 8–9 hours

Bioavailability: - 85% - 95%

Absorption: - approximately 98% **[32]**

PH: - 2 and 5 and sparingly to slightly soluble in aqueous solutions with pH 7 (solubility falls to 4 mg/mL)**[33]**

LogP/**Hydrophobicity: -** 2.1**[32]**

PKa: - 40**[34]**

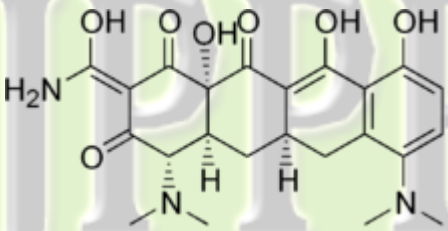
Dissolution: - Ofloxacin Tablet [35]

Medium: - 0.1N Hcl [900ml]

Apparatus: - I (Basket)

Rpm: - 100

Minocycline [36]



Systematic (IUPAC) name: - (2*E*,4*S*,4a*R*,5aS,12a*R*)- 2-(amino-hydroxy-methylidene)- 4,7-bis(dimethylamino)-10,11,12a-trihydroxy-4a,5,5a,6- tetrahydro-4H-tetracene-1,3,12-trione.

Chemical data: -

Formula: - $C_{23}H_{27}N_3O_7$

Mol. Mass: - 457.477

Description: -Yellow, crystalline powder.**[USP][37]**

Solubility profile: -Sparingly soluble in water, soluble in solution of alkali hydroxides and carbonates, slightly soluble in alcohol, practically insoluble in chloroform and in ether.**[USP] [37]**

Melting Point : - 104 - 110°C**[38]**

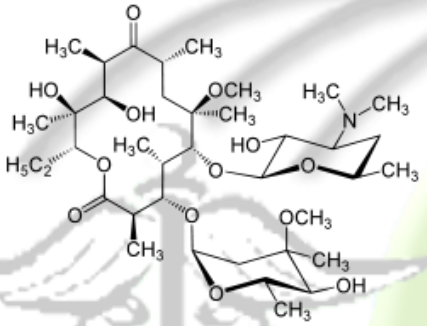
Pharmacology: -

Mechanism of Action: - Minocycline passes directly through the lipid bilayer or passively diffuses through porin channels in the bacterial membrane. Tetracyclines like minocycline bind to the 30S ribosomal subunit, preventing the binding of tRNA to the mRNA-ribosome complex and interfering with protein synthesis.**[39]**

Pharmacokinetic data: -

Bioavailability: - 100%

Metabolism: - liver
Half-life: - 11-22 hours
Excretion: - mostly fecal, rest renal
Biotransformation: - Hepatic **[39]**
Ph: - 3.5-4.5**[38]**
LogP/**Hydrophobicity: -** Hepatic**[39]**
pKa: - *pKa*1 = 2.8**[40]**
*pKa*2 = 5.0;
*pKa*3 = 7.8
*pKa*4 = 9.3
Dissolution:- Minocycline ER Tablets [41]
Medium: - 0.1N Hcl[900 ml]
Apparatus: - 1
Rpm: - 100
Clarithromycin [42]



Systematic (IUPAC) name: -
(3*R*,4*S*,5*S*,6*R*,7*R*,9*R*,11*S*,12*R*,13*S*,14*S*)-6-{[(2*S*,3*R*,4*S*,6*R*) -4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy} -14-ethyl-12,13-dihydroxy-4-{[(2*R*,4*S*,5*S*,6*S*)-5-hydroxy -4-methoxy-4,6-dimethyloxan-2-yl]oxy}-7 -methoxy-3,5,7,9,11,13-hexamethyl -1-oxacyclotetradecane-2,10-dione
Chemical data: -
Formula: - $C_{38}H_{69}NO_{13}$
Mol. Mass: - 747.953 g/mol
Melting Point : - 220 C**[43]**
Description: -White to off white, crystalline powder.**[USP][44]**
Solubility profile: -Soluble in acetone, slightly soluble in dehydrated alcohol, in methanol and in acetonitrile. Practically insoluble in water, slightly soluble in phosphate buffer at Ph values of 2 to 5.**[USP][44]**
Solubility profile: -Practically insoluble in water, soluble in acetone and methylene chloride, slightly soluble in methanol.**[IP][45]**
Pharmacology: -
Mechanism of Action: - Clarithromycin is first metabolized to 14-OH clarithromycin. Like other macrolides, it then binds to the 50 S subunit of the 70 S ribosome of the bacteria, blocking RNA-mediated bacterial protein synthesis. Clarithromycin also inhibits the hepatic microsomal CYP3A4 isoenzyme and P-glycoprotein, an energy-dependent drug efflux pump.**[46]**

Pharmacokinetic data
Bioavailability: - 50%
Protein binding: -low binding
Metabolism: - hepatic
Half-life: - 3-4 hours
LogP/**Hydrophobicity: -** 3-4 hours **[46]**
Ph: - 8.0 - 10.0**[43]**
pKa: - 9.0**[47]**
Dissolution: - Clarithromycin Extended drug release tablet[48]
Rpm: - 75
Medium: - 0.3 M phosphate buffer, pH 6.0 (prepared by dissolving 816.5 g of monobasic potassium phosphate and 48 g of sodium hydroxide in about 4 L of water, mixing, and diluting with water to 20 L. Adjust with either concentrated phosphoric acid or 1 N sodium hydroxide to a pH of 6.0 ± 0.05); 900 mL.
Apparatus: - 2
Referance: -

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