Chapter – 2

LITERATURE REVIEW
2.1. PAST REVIEWS ON NEED OF CONTROLLED RELEASE FORMULATIONS OF ARV’s

- Sosnik A et al., (8) reported that state-of-the-art ARV DDS and thoroughly discussed the challenges in the development of medicines with enhanced biopharmaceutical properties. In this context, DDS research is poised to become the tool to develop safe, stable, easy-to-use and more importantly, economically affordable treatments. Thus, it is stated that there is a need for the development of such novel drug development on the Pharmaceutical technology field.

- Ojewole E et al., (9) reported the various ARV delivery systems that have been developed for achieving sustained drug release kinetics, specifically targeting drugs and for addressing formulation difficulties such as poor solubility, stability and drug entrapment. The physicochemical properties and the in vitro/in vivo performances of various systems were summarized. Thus, based on the complexity of the disease and the formulation optimization and evaluation studies required, multidisciplinary research would be essential for eventual commercialization of NDDS containing ARV drugs.

- Devi KV et al., (10) reported that Human Immunodeficiency Virus is a retrovirus that causes irreversible destruction of the immune system, leading to the occurrence of opportunistic infections and malignancies. Delivery systems for these drugs are being developed to compensate the shortcomings. However, the benefits of technological advancements are yet to reach the poor and needy patients.

2.2. PAST STUDIES ON LAMIVUDINE CONTROLLED RELEASE FORMULATIONS

- Parveen A et al., (33) worked out on preparation and evaluation of mucoadhesive microspheres of Lamivudine. The particle size, drug excipients compatibility by FTIR, % drug content, Entrapment efficiency and in vitro dissolution studies, and SEM were determined.

- Katakam P et al., (34) evaluated the oral extended release matrix tablets of Lamivudine, using HPMC K100M and in combination with PEO as release rate retardant polymers, for in vitro dissolution and in vivo bioavailability performance in rabbits. In vitro studies revealed that the release rate decreased with increase in polymer concentration, viscosity and combination of polymers.
Singh AV et al., (35) reported that the development of controlled release tablets of Lamivudine with the cross-linked derivative was synthesized with phosphorous oxychloride and native sago starch in the basic pH medium. The formulated tablets were evaluated for various physical characteristics, in vitro dissolution release study and in vivo pharmacokinetic study in a rabbit model.

Singh B et al., (36) reported the preparation and evaluation gastro retentive tablets of Lamivudine effervescent floating-bio adhesive hydrophilic matrices. Pharmacokinetic studies were carried out in rabbits, and various levels of in vitro/in vivo correlation were established.

Apparao P et al., (37) aimed at formulating and evaluating gum based sustained release matrix tablets of Lamivudine using different natural polymers such as Guar gum, Xanthan gum, Rosin gum, Pectin, and Sodium alginate taken at 30%, 40% and 50% of the total weight of the tablet.

Arkhel A et al., (38) reported that the possibilities of using tamarind seed polysaccharide in industries with particular reference to its physical, chemical properties for the formation of new drug delivery systems. The in vivo investigation in rabbits showed sustained release pharmacokinetic profile of Lamivudine up to 24 hours.

Singh MN et al., (39) reported the general aspects and recent advances in drug loaded microparticles. The microcapsules and microspheres can be used not only for controlling release but also for targeted delivery of drugs to a specific site in the body.

Raju PN et al., (40) reported the influence of tablet surface area/volume on drug release from extended release matrix of tablets of Lamivudine prepared with HPMC.

Tamizhrasi S et al., (41) reported the preparation and evaluation of polymethacrylic acid nanoparticles containing Lamivudine in different drug to polymer ratio by nanoprecipitation method. The slow and constant release of Lamivudine from nanoparticles maintain constant drug plasma concentration thereby increasing therapeutic efficacy.

Prakash K et al., (42) reported that microcapsules for the controlled release of Lamivudine using various cellulose polymers. The release kinetics data and characterization studies indicate that drug release from microcapsules was diffusion controlled and the microcapsules were stable.
Ravi PR et al., (43) reported that oral controlled release matrix tablets of Lamivudine using HPMC as the retardant polymer and to study the effect of various formulation factors. In vitro release studies revealed that the release rate decreased with increase in polymer proportion and viscosity grade.

Ghosh A et al., (44) reported the preparation, evaluation of Lamivudine incorporated microspheres composed of ethyl cellulose as a release controlling polymer.

2.3. PAST STUDIES ON NATURAL GUMS AS RELEASE RATE RETARDING POLYMERS

Choudhary PD et al., (45) reported that the use of natural gums for pharmaceutical applications is attractive because they are economical, readily available, nontoxic, capable of chemical modifications, potentially biodegradable, and with few exceptions, also biocompatible. There is huge scope for research on newer gums and mucilages obtained from plants and could be further exploited in future as a novel natural polymer for the development of different DDS in the pharma industry.

Panda DS et al., (46) reported that a preformulation study on the gum of Moringa oleifera. The results were found favorable with rheological and compatibility studies. It appears that the gum has the potential candidate to be used as an excipient in different pharmaceutical dosage forms.

Shivalingam MR et al., (47) reported that the gum isolated from the stem of Moringa oleifera have been evaluated for its binding properties in the formulation of conventional paracetamol tablet (500mg) containing 8%, 10% and 12% binding concentration. From the studies, it is concluded that an increase in binding concentration decreases drug release; hence, this gum can be used to formulate sustained/controlled release tablet formulation.

Panda DS et al., (48) reported that the potential of gum from Moringa oleifera to act as a binder and release retardant in tablet formulations.

Panda D et al., (49) reported that preparation and evaluation of gels from the gum of Moringa oleifera. Seven batches of drug loaded gels with mucilage ranging from 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, and 8.5 were formulated. The pH, viscosity, and in vitro diffusion profiles were studied. The gels prepared with 8.0% of mucilage were found to be ideal and comparable with a commercial preparation.
Gowthamarajan K et al.,\(^{(50)}\) reported that development of unidirectional, bilayered, mucoadhesive tablets of curcumin, along with ethyl cellulose as an impermeable backing layer using *Anacardium occidentale* gum. The results suggest that cashew nut tree gum can be used as a polymer to produce mucoadhesive tablets of curcumin, to bypass the first pass metabolism and improve the bioavailability of curcumin.

Kumar A et al.,\(^{(51)}\) reported that the Cashew gum (bark exudate from *Anacardium occidentale*) can be used as a versatile polymer. Thus, this novel polymer can become a candidate of major interest in recent years because of its potential applications in several fields.

Gowthamarajan K et al.,\(^{(52)}\) reported the Preliminary study of *Anacardium occidentale* gum as a binder in the formulation of paracetamol tablets. The result suggests that cashew nut tree gum can be used as an alternative binder with 2.5% concentration to produce a tablet of better mechanical strength.

Kumar R et al.,\(^{(53)}\) reported the binding potentials of a natural gum obtained from plant *Anacardium occidentale*. The mucilage was evaluated for its granulating and binding properties in tablets, using diclofenac as a model drug. At 6% concentration, it has given similar disintegration time and dissolution profile in comparison to starch at 10% w/v.

Igwe OU et al.,\(^{(54)}\) reported that the cassava and maize starches were used in combination with gum to investigate certain physicochemical properties. The addition of *Delonix regia* gum to cassava and maize starches at a low concentration of 0.2% caused a significant decrease in peak viscosity and paste clarity and improved freeze-thaw stability of the starches, to improve their functional characteristics for specific food and industrial application.

Sarangapani S et al.,\(^{(55)}\) were reported the development and characterization of the sustained release matrix tablet of lansoprazole prepared by the wet granulation method using novel polymeric material from *Delonix regia*.

Tekade AR et al.,\(^{(56)}\) reported that development of a pulsatile drug delivery system based on an insoluble capsule body filled with theophylline microspheres and sealed with a swellable novel polymer plug isolated from the endosperm of seeds of higher plant *Delonix regia* family Fabaceae.
2.4. LITERATURE ON EMBEDMENT TECHNIQUE

- Ho-Wah Hui et al., (26) reported that among the newer emerging technologies for designing, controlling drug delivery systems with improved efficiency and embedment is one such novel technique. The release rate retarding material or polymer is the major component of these systems and its concentration influences the release rate of the drug.

2.5. PAST STUDIES ON CONTROLLED RELEASE FORMULATIONS OF EMTRICITABINE

- Singh G et al., (57) reported the development of nanoparticles of Emtricitabine solely using poly(lactic co- glycolic acid) and evaluate it in vitro and in vivo release performance by a systematically optimized HPLC method using Formulation by Design.

- Hussain ZH et al., (58) reported the development of a pharmaceutical stable, cost effective and quality improved formulation of Emtricitabine delayed-release tablets. Twelve formulations of enteric coated tablets of Emtricitabine were developed by the direct compression method.

- Fathima A et al., (59) reported that the microparticles loaded with Emtricitabine were formulated through ionotropic gelation method using sodium alginate as retardant polymer and calcium chloride as a crosslinker.

2.6. PAST STUDIES ON COMPRESSION COATING TECHNOLOGY FOR CONTROLLED RELEASE

- Jaimini M et al., (60) reported the general characteristics, introduction, classification and formulation consideration of compression coating tablet. Drug release of compression-coated tablets as extended release can be modified by adjusting drug-polymer ratio in core and coat.

- Banerjee MN et al., (61) reported the formulation cefpodoxime proxetil compression-coated tablets for gastro retentive drug delivery. In this, the tablet is formulated to be retained in the stomach for a period of approximately 12 hrs using different polymer blend.

- Rajendra A et al., (62) reported the study of fast disintegrating core tablets of model drug diclofenac sodium were coated with coating material granules containing okra mucilage in combination with HPMC K15M and evaluated for pre and post compression parameters.
Fukui E et al., (63) reported the preparation of press coated tablets, containing diltiazem hydrochloride in the core tablet and coated with hydroxypropyl cellulose as the outer shell, were examined for applicability as timed release tablets with a predetermined lag time and subsequent rapid drug release phase.

2.7. PAST STUDIES ON POLYMERS FOR CONTROLLED RELEASE

Murtaza G (64) reported the EC based microencapsulated drug delivery systems were being extensively studied throughout the world for achieving extended drug release and protecting the core substance from degradation. Drug release is decreased with increasing molecular weight (viscosity) of the EC.

Rogers TL et al., (65) reported that ethyl cellulose, methyl cellulose and hypromellose were used to make microcapsules. It also discusses various materials used to formulate microcapsules, such as the three encapsulating polymers as well as protective colloids, plasticizers and surfactants, various techniques used to make microcapsules, such as temperature induced phase separation, emulsion solvent evaporation, solvent evaporation, film coating, and others and various applications for which microcapsules are used, such as modified release, improved efficacy and safety, taste and odor masking.

Pandit SS et al., (66) reported that Eudragit RSPO microspheres containing ketoprofen as a model drug, prepared by solvent evaporation technique using acetone, the liquid paraffin (heavy) solvent system were examined.

Vaghani S et al., (67) reported the preparation and evaluation of microspheres of Eudragit (RS, RL and RSPO) containing an anticancer drug 5-Fluorouracil. Microspheres were prepared and evaluated for Mean particle size, entrapment efficiency and production yield were highly influenced by the type of polymer and polymer concentration.

Khamanga SM et al., (68) reported the preparation of microcapsules containing verapamil and propranolol and evaluation of kinetics and mechanism of drug release from the microcapsules using USP Apparatus I. The microcapsules were manufactured using Eudragit RS and RL polymers.

2.8. PAST STUDIES ON COMBINATION OF LAMIVUDINE WITH TENOFOVIR DF & EMTRICITABINE WITH TENOFOVIR DF

Nanaji PS et al., (69) reported the formulation and evaluation an immediate release tablet of Lamivudine and Tenofovir DF using different disintegrants by direct compression method.
Feleder EC et al., (70) reported the comparison of the rate and extent of absorption and to assess the bioequivalence between a new pharmaceutical equivalent tablet formulation containing a fixed-dose combination of Tenofovir DF/Lamivudine 300/300 mg and the innovator products.

Srilatha U et al., (71) reported the formulation and evaluation of once-daily an immediate release tablet of Emtricitabine and Tenofovir DF. Tablets formulated using different disintegrants by direct compression technique.

Reddy BV et al., (72) reported the formulation of the film coated tablets of Emtricitabine and Tenofovir DF, drugs which are used in the treatment of HIV-1 infection.

2.9. PAST STUDIES ON TABLETTING OF MICROCAPSULES

Hu X et al., (73) reported that the preparation and evaluation of a taste-masked berberine hydrochloride orally disintegrating tablet contain microcapsules for enhanced patient compliance. This technology can be applied to other bitter-tasting drugs.

Karasulu HY et al., (74) reported that microcapsules of ketoconazole with 1:1 and 1:2 core wall ratios were prepared by means of the phase separation technique using sodium carboxymethyl cellulose as a coating material. In addition, to evaluate whether some kind of glidant will be needed during tabletting of microcapsules, the Hausner’s ratio and consolidation index were also calculated and it may be concluded that microcapsules do not need any glidant.

2.10. PAST STUDIES ON BILAYERED TABLETS FOR CONTROLLED RELEASE

Ryakala H et al., (75) stated that the combination of Nebivolol and Nateglinide can be used for better patient compliance. IR layer was formulated using various super disintegrants and SR layer was formulated using polymers and gums.

Natarajan R et al., (76) reported that development of trilayer and bilayer tablets show a good initial release of Nevirapine and sustained release of Zidovudine and Lamivudine. The results demonstrate that the release profile strongly dependent on the ratio of drug to polymer and independent of separation of layers.

Patra C et al., (77) developed a bilayer tablet of propranolol hydrochloride using super disintegrant sodium starch glycolate for the fast release layer and water immiscible polymers such as ethylcellulose, Eudragit RLPO and Eudragit RSPO for the sustaining layer.
2.11. LITERATURE ON LAMIVUDINE (1-6, 78, 79)

2.11.1. Lamivudine – A profile

Lamivudine is the pyrimidine-based nucleoside analogue. Lamivudine (3TC) is an antiretroviral drug known as potent nucleoside analogue reverse transcriptase inhibitor, which blocks reverse transcriptase, an enzyme crucial to viral production in HIV-infected people. It was approved by the U.S. Food and Drug Administration for the treatment of HIV and Hepatitis B

2.11.2. General and Physicochemical properties

- **Synonyms**: 2',3'-Dideoxy-3'-thiacytidine, 3TC, BCH 189
- **Brand Names**: Epivir, Zeffix, Heptovir
- **Chemical class**: 3'-thia pyrimidine nucleoside analogue
- **Chemical Structure**: ![Chemical Structure of Lamivudine](image)

**Figure 2.1: Chemical Structure of Lamivudine**

- **IUPAC Name**: 4-amino-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]1,2- dihydropyrimidin-2-one
- **Molecular Formula**: C₈H₁₁N₃O₃S.
- **Molecular Mass**: 229.26 g/mol
- **Physical Appearance**: A white to almost white crystalline solid
- **Melting point**: 172-178 °C
- **Solubility**: Soluble in water; Sparingly soluble in methanol; Practically insoluble in acetone
- **BCS Class**: Class I
- **Therapeutic Class**: Anti-viral agent.
- **Therapeutic Use**: For the treatment of HIV-1 infection & Hepatitis-B
2.11.3. Clinical Pharmacology

- **Mechanism of action:** Lamivudine is a nucleoside reverse transcriptase inhibitor (NRTI) with activity against Human Immunodeficiency Virus Type 1 (HIV-1) and hepatitis B (HBV). Lamivudine is an analogue of cytidine. It is phosphorylated to active metabolites, Lamivudine triphosphate (L-TP) and Lamivudine monophosphate (L-MP) that compete for incorporation into viral DNA. They inhibit the HIV reverse transcriptase enzyme competitively and act as a chain terminator of DNA synthesis. The lack of a 3’-OH group in the incorporated nucleoside analog prevents the formation of the 5’ to 3’ phosphodiester linkage essential for DNA chain elongation, and therefore, the viral DNA growth is terminated.

2.11.4. Pharmacokinetic properties:

- **Absorption:** Lamivudine is well absorbed from the gastrointestinal tract, and the bioavailability of oral Lamivudine in adults is normal between 80 and 85%. When given with food, absorption is slower, compared to the fasted state.

- **Distribution:** From intravenous studies, the mean volume of distribution is 1.3L/kg. The observed half-life of elimination is 5 to 7 hours. Lamivudine exhibits linear pharmacokinetics over the therapeutic dose range and displays limited binding to the major plasma protein albumin.

- **Metabolism:** The active moiety, intracellular Lamivudine triphosphate, has a prolonged terminal half-life in the cell (16 to 19 hours) compared to the plasma Lamivudine half-life (5 to 7 hours).

- **Excretion:** The mean systemic clearance of Lamivudine is approximately 0.32 L/h/kg, with predominantly renal clearance (> 70%) via the organic cationic transport system. The majority of Lamivudine is eliminated unchanged in urine by active organic cationic secretion.

**The summary of pharmacokinetic parameters**

- **C<sub>max</sub>** : 1.2µg/mL (150mg bd dosing, healthy subjects); 2.0µg/mL (300mg od dosing, healthy subjects).

- **C<sub>min</sub>** : 0.09µg/mL (150mg bd dosing, healthy subjects); 0.04µg/mL (300mg od dosing, healthy subjects).

- **AUC** : 4.7µg.h/mL (150mg bd dosing, healthy subjects); 8.9µg.h/mL (300mg od dosing, healthy subjects).
Bioavailability: 80-85%
Protein binding: <36% bound to plasma protein.
Volume of Distribution: 1.3 L/kg.
CSF: Plasma Ratio: ~0.12
Semen: Plasma Ratio: 9.1 (2.3-16.1)
Renal clearance: >70%

2.11.5. Side Effects:
Abdominal or stomach discomfort, black, tarry stools, bleeding gums, bloating, blood in the urine or stools, chills, indigestion, muscle or joint pain, sensation of pins and needles, sore throat, stabbing pain, stomach discomfort, upset, or pain, stuffy or runny nose, trouble sleeping, weight loss.

2.11.6. Contraindications:
- Lamivudine and zidovudine fixed dose combination tablet should not be administered concomitantly with Lamivudine tablets or Lamivudine oral solution.
- In one small study, concurrent administration of sulfamethoxazole and trimethoprim combination resulted in a 44% increase in Lamivudine AUC and a decrease of 29% in Lamivudine oral clearance and a 30% decrease in Lamivudine renal clearance.
- Lamivudine and zalcitabine may inhibit the phosphorylation of one another and concurrent administration is not recommended.

2.11.7. Adverse Drug Reactions:
Severe adverse reactions of Lamivudine include Lactic acidosis and severe hepatomegaly with steatosis, Severe acute exacerbations of hepatitis B. Common adverse reactions include Headache, insomnia, cough, nasal symptoms, nausea, vomiting, abdominal pain or cramps, diarrhoea, rash, alopecia, arthralgia, muscle disorders.

2.11.8. Drug interactions:
- The possibility of interactions with other drugs administered concurrently should be considered, particularly when their main route of elimination is active renal secretion via the organic cationic transport system (e.g., trimethoprim).
- Interferon- And Ribavirin-Based Regimens: Hepatic decompensation (some fatal) has occurred in HIV-1/HCV co-infected patients receiving combination antiretroviral therapy for HIV-1 and interferon alfa with or without ribavirin.
• Zalcitabine: Lamivudine and zalcitabine may inhibit the intracellular phosphorylation of one another. Therefore, use of Lamivudine in combination with zalcitabine is not recommended.

2.11.9. Dosage and Administration:

a) Adult Patients: The recommended oral dose of Lamivudine tablets in HIV-1-infected adults is 300 mg daily, administered as either 150 mg twice daily or 300 mg once daily, in combination with other antiretroviral agents.

b) Pediatric Patients: Lamivudine tablets are available as scored tablets for HIV-1-infected pediatric patients who weigh at least 14 kg and for whom a solid dosage form is appropriate. Before prescribing Lamivudine tablets, children should be assessed for the ability to swallow tablets. If a child is unable to reliably swallow Lamivudine tablets, the oral solution formulation should be prescribed.

Table 2.1: Dosing Recommendations for Lamivudine Scored (150 mg) Tablets in Pediatric Patients

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Twice-daily Dosing Regimen Using Scored 150 mg Tablet</th>
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<tbody>
<tr>
<td></td>
<td>AM Dose</td>
</tr>
<tr>
<td>14 to &lt;20</td>
<td>½ tablet (75 mg)</td>
</tr>
<tr>
<td>14 to &lt;20</td>
<td>½ tablet (75 mg)</td>
</tr>
<tr>
<td>≥25</td>
<td>1 tablet (150 mg)</td>
</tr>
</tbody>
</table>

2.11.10. Overdose:

Administration of Lamivudine at very high dose levels in acute animal studies did not result in any organ toxicity. Since Lamivudine is dialyzable, continuous haemodialysis could be used in the treatment of overdosage.

2.11.11. Uses:

Lamivudine is indicated in the treatment of chronic hepatitis B associated with evidence of hepatitis B viral replication and active liver inflammation. This use is based on 1-year histologic and serologic responses in patients with compensated chronic hepatitis B.
2.12. LITERATURE ON EMTRICITABINE (1-6, 78, 79)

2.12.1. Emtricitabine – A profile

Emtricitabine is the pyrimidine-based nucleoside analogue. Emtricitabine (FTC) is an antiretroviral drug known as potent nucleoside analogue reverse transcriptase inhibitor, which blocks reverse transcriptase, an enzyme crucial to viral production in HIV-infected people. It was approved by the U.S. Food and Drug Administration for the treatment of HIV.

2.12.2. General and Physicochemical properties

- **Synonyms**: FTC, Emtricitabin, 5-fluoro-3'-thiacytidine
- **Brand Names**: Emtriva, Truvada (Emtricitabine + Tenofovir DF)
- **Chemical Class**: 3'-thia pyrimidine nucleoside analogue
- **Chemical Structure**

![Figure 2.2: Chemical Structure of Emtricitabine](image)

- **IUPAC Name**: 4-amino-5-fluoro-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one
- **Molecular Formula**: C₈H₁₀FN₅O₃S
- **Molecular Mass**: 247.247 g/mol
- **Physical Appearance**: White to off-white crystalline powder.
- **Melting point**: 148-156 °C
- **Solubility**: Soluble in water; Sparingly soluble in methanol; Practically insoluble in acetone
- **BCS Class**: Class I
- **Therapeutic Class**: Antiretroviral agent
- **Therapeutic Use**: For the treatment of HIV-1 infection in adults.
2.12.3. Clinical Pharmacology:

- **Mechanism of Action:** Emtricitabine, a synthetic nucleoside analog of cytidine, is phosphorylated by cellular enzymes to form Emtricitabine 5'-triphosphate. Emtricitabine 5'-triphosphate inhibits the activity of the HIV-1 RT by competing with the natural substrate deoxycytidine 5'-triphosphate and by being incorporated into nascent viral DNA which results in chain termination. Emtricitabine 5’-triphosphate is a weak inhibitor of mammalian DNA polymerase α, β, ε, and mitochondrial DNA polymerase γ.

2.12.4. Pharmacokinetic properties:

- **Absorption:** Emtricitabine is rapidly absorbed with peak plasma concentrations occurring at 1–2 hours post-dose. The mean absolute bioavailability of Emtricitabine was 93%.

- **Distribution:** *In vitro* binding of Emtricitabine to human plasma proteins was <4% and independent of concentration over the range of 0.02–200 g/mL.

- **Metabolism:** Emtricitabine is not an inhibitor of human CYP450 enzymes. Upon administration of C-Emtricitabine, complete recovery of the dose was achieved in urine (~86%) and feces (~14%). 13% of the dose was recovered in urine as three putative metabolites. The biotransformation of Emtricitabine includes oxidation of the thiol moiety to form the 3’-sulfoxide diastereomers (~9% of dose) and conjugation with glucuronic acid to form 2’-O-glucuronide (~4% of dose).

- **Excretion:** Emtricitabine is eliminated by a combination of glomerular filtration and active tubular secretion through the urine (86%, with 13% as putative metabolites) and feces (14%).

The summary of pharmacokinetic parameters (81):

- $C_{\text{max}}$ : 1.8 ± 0.7 µg/mL (200 mg of od dosing, HIV-infected subjects).
- $C_{\text{min}}$ : 0.09±0.07µg/mL (200 mg of od dosing, HIV-infected subjects)
- AUC : 10 ±3.1µg.h/mL (200 mg of od dosing, HIV-infected subjects).
- **Bioavailability** : 93% (hard capsules)
- **Protein Binding** : Very low (less than 4%).
- **Volume of Distribution** : 1.4 ± 0.3L/kg.
- **CSF:Plasma Ratio** : 0.43
- **Semen:Plasma Ratio** : ~4.0.
- **Renal clearance** : ~86%
2.12.5. Side Effects:

Burning, crawling, itching, numbness, prickling, or tingling feelings, cough or hoarseness, fever or chills, painful or difficult urination, pale skin, troubled breathing with exertion, unusual bleeding or bruising, unusual tiredness or weakness.

2.12.6. Contraindications

Emtricitabine is not significantly metabolized by liver enzymes, so the impact of liver impairment should be limited. Symptoms of overdose include serious liver problems (hepatotoxicity, with liver enlargement and fat in the liver called steatosis) or a lactic acidosis (buildup of an acid in the blood).

2.12.7. Adverse Drug Reactions:

- Severe acute exacerbation of hepatitis can occur in hepatitis B virus (HBV)-coinfected patients who discontinue Emtricitabine.
- Hyperpigmentation/skin discoloration on palms and/or soles.

2.12.8. Drug Interactions:

Do not take this medication if you are already taking Atripla, Complera, Truvada, Combivir, Epivir, Epivir-HBV, Epzicom, Trizivir because these medicines contain the same or similar active ingredient.

2.12.9. Dosage and Administration:

- Capsules: one 200 mg capsule administered once daily orally.
- Oral solution (10 mg/mL): 240 mg (24 mL) administered once daily orally.

2.12.10. Overdose

There is no known antidote for Emtricitabine. No severe adverse reactions were reported with overdose. If overdose occurs the patient should be monitored for signs of toxicity, and standard supportive treatment applied as necessary. Hemodialysis treatment removes approximately 30% of the Emtricitabine dose over a 3-hour dialysis period starting within 1.5 hours of Emtricitabine dosing (blood flow rate of 400 mL/min and a dialysate flow rate of 600 mL/min).

2.12.11. Uses:

Emtricitabine is used with other HIV medications to help control HIV infection. It helps to decrease the amount of HIV in your body so your immune system can work better. This lowers your chance of getting HIV complications (such as new infections, cancer) and improves your quality of life. Emtricitabine belongs to a class of drugs known as nucleoside reverse transcriptase inhibitors-NRTI.
2.13. LITERATURE ON TENOFOVIR DISOPROXIL FUMARATE (1-6, 78, 79)

2.13.1. Tenofovir DF – A profile

Tenofovir disoproxil fumarate is the salt of Tenofovir disoproxil with fumaric acid. Tenofovir disoproxil is a diester prodrug of the purine-based nucleotide analogue, Tenofovir. The pro-drug has increased oral bioavailability compared to Tenofovir. Tenofovir Disoproxil Fumarate is an antiretroviral drug known as nucleotide analogue reverse transcriptase inhibitor (NtRTI), which blocks reverse transcriptase, an enzyme crucial to viral production in HIV-infected people. It was approved by the U.S. Food and Drug Administration for the treatment of HIV and chronic hepatitis B.

2.13.2. General and Physicochemical properties:

- **Synonyms**: Tenofovir disoproxil, PMPA
- **Brand names**: Viread
- **Chemical class**: 6-aminopurine class
- **Chemical Structure**:

![Chemical structure of Tenofovir DF](image)

**Figure 2.3: Chemical structure of Tenofovir DF**

- **Molecular Formula**: C_{19}H_{30}N_{5}O_{10}P•C_{4}H_{4}O_{4}
- **Molecular Mass**: 635.51g/mol
- **Physical Appearance**: White to off-white crystalline powder
- **Melting point**: 114-116 °C
- **Solubility**: Soluble in DMSO, methanol, water and ethanol.
- **BCS Class**: Class 3
- **Therapeutic Class**: Antiretroviral Agent
- **Therapeutic Use**: To treat HIV/AIDS and chronic hepatitis B.
2.13.3. Clinical Pharmacology:

- **Mechanism of action:** Tenofovir inhibits the activity of HIV reverse transcriptase by competing with the natural substrate deoxyadenosine 5’-triphosphate and, after incorporation into DNA, by DNA chain termination. NRTIs and NtRTIs (nucleoside/tide reverse transcriptase inhibitors) lack a 3’-hydroxyl group on the deoxyribose moiety. As a result, following incorporation of an NRTI the next incoming deoxynucleotide cannot form the next 5’-3’ phosphodiester bond needed to extend the DNA chain.

2.13.4. Pharmacokinetic properties:

- **Absorption:** The oral bioavailability in fasted patients is approximately 25%. Administration of Tenofovir DF with a high fat meal increased Tenofovir AUC by approximately 40% and Cmax by approximately 14%.
- **Distribution:** Volume of distribution is approximately 1.3 L/kg. Binding to plasma or serum proteins is less than 0.7% and 7.2%, respectively.
- **Metabolism:** The cytochrome P450 enzyme system is not involved in the metabolism of Tenofovir DF. Adenylate kinase isoenzyme 1 and mitochondrial Adenylate kinase 2 converts Tenofovir to Tenofovir monophosphate and subsequently into Tenofovir diphosphate.
- **Excretion:** Tenofovir is eliminated by a combination of glomerular filtration and active tubular secretion through urine. The terminal elimination half-life is approximately 17 hours.

**The summary of pharmacokinetic parameters** (82)

- $C_{\text{max}}$ : 326ng/ml (HIV infected patients)
- $C_{\text{min}}$ : 64.4ng/ml (HIV infected patients)
- AUC : 3324ng.h/ml (HIV infected patients)
- Bioavailability : 25%
- Protein Binding : Very low.
- Volume of Distribution: ~0.8L/kg
- CSF: Plasma Ratio : Believed to below to anionic charge of the molecule at physiological pH
- Semen: Plasma Ratio: Accumulate in semen at higher conc. than plasma.
- Renal clearance : 70-80% as unchanged drug
2.13.5. Side Effects:

Tenofovir DF can cause severe side effects. These include lactic acidosis and severe liver problems. Other possible side effects of Tenofovir DF include: New or worsening kidney problems, Bone problems, including bone pain, softening, or thinning (osteopenia), which may lead to fractures, Changes in body fat (lipodystrophy), Immune reconstitution inflammatory syndrome (IRIS), a condition that sometimes occurs when the immune system begins to recover after treatment with an HIV medicine.

2.13.6. Contraindications:

Broken Bone due to Disease or Illness, Enlarged Fatty Liver, Acute Kidney Disease, Kidney Disease, Decreased Calcification or Density of Bone, A Mother who is Producing Milk and Breastfeeding, Softening of Bones, Low Amount of Phosphate in the Blood, Increased Blood Acidity due to High Levels of Lactic Acid, Fanconi’s Syndrome.

2.13.7. Adverse Drug Reactions:

- Gastrointestinal events such as anorexia, abdominal pain, diarrhoea, dyspepsia, flatulence, nausea, and vomiting other common reported adverse effects are dizziness, fatigue, and headache skin rashes may occur.
- Renal effects, including nephritis, Lactic acidosis usual associated with severe hepatomegaly and steatosis may occur.
- Metabolic abnormalities such as hypertriglyceridaemia, hypercholesterolemia, insulin resistance, hyperglycemia, and hyperlactatemia have also been reported.
- Elevated creatine phosphokinase, myalgia myositis, and rarely rhabdomyolysis have been reported, particularly in patients with advanced HIV disease or long-term exposure to combination antiretroviral therapy.

2.13.8. Drug Interactions:

- Acyclovir: Acyclovir-Valacyclovir may decrease the excretion of Tenofovir.
- Adefovir, Dipivoxil: Adefovir may diminish the therapeutic effect of Tenofovir. Specifically, adefovir-associated mutations in Hepatitis B viral reverse transcriptase may decrease viral susceptibility to Tenofovir. Tenofovir may increase the serum concentration of Adefovir. Adefovir may increase the serum concentration of Tenofovir.
• Amikacin: May increases the serum concentration of Aminoglycosides which may increase the serum concentration of Tenofovir.
• Arbekacin: Tenofovir may increase the serum concentration of Aminoglycosides. Aminoglycosides may increase the serum concentration of Tenofovir.
• Atazanavir: Tenofovir may decrease the serum concentration of Atazanavir. Atazanavir may increase the serum concentration of Tenofovir.
• Celecoxib: Nonsteroidal Anti-Inflammatory Agents may enhance the adverse/toxic effect of Tenofovir.
• Cidofovir: May decreases the excretion of Tenofovir.
• Cobicistat: May enhances the adverse/toxic effect of Tenofovir. More specifically, Cobicistat may impair proper Tenofovir monitoring and dosing.
• Darunavir: Tenofovir may increase the serum concentration of Darunavir. Darunavir may increase the serum concentration of Tenofovir.
• Diclofenac: Diclofenac (Systemic) may enhance the adverse/toxic effect of Tenofovir.

2.13.9. Dosage and Administration:
• Adults: in adults and pediatric patients 12 years of age and older (35 kg or more): 300 mg once daily taken orally without regard to food.
• Pediatrics: in pediatric patients (2 to less than 12 years of age): Tablets: for pediatric patients weighing greater than or equal to 17 kg who can swallow an intact tablet, one VIREAD tablet (150, 200, 250 or 300 mg based on body weight) once daily taken orally without regard to food or Oral powder: 8 mg/kg VIREAD oral powder (up to a maximum of 300 mg) once daily with food.

2.13.10. Overdose:

Limited clinical experience at doses higher than the therapeutic dose of VIREAD 300 mg is available. No severe adverse reactions were reported. The effects of higher doses are not known. Tenofovir is efficiently removed by hemodialysis with an extraction coefficient of approximately 54%.

2.13.11. Uses:

It is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 2 years of age and older. It is indicated for the treatment of chronic hepatitis B in adults and pediatric patients 12 years of age and older.
2.14. LITERATURE ON MORINGA OLIEFERA GUM (46-49)

❖ **Common name**

    Drumstick tree gum

❖ **Taxonomy**

    - Phylum : Tracheophyta
    - Class : Magnoliopsida
    - Order : Brassicales
    - Family : Moringaceae
    - Genus : Moringa

❖ **Description**

    Yellow to pale yellow coloured, odourless fine powder.

❖ **Composition**

    It is a polyuronide constituting of arabinose, galactose and glucuronic acid in
    the preparation of 10:7:2, rhamnose present in traces.

❖ **Physicochemical parameters**

    - Loss on drying : 12.02%
    - Total ash : 12%
    - Acid soluble ash : 3%
    - pH : 6.8 - 6.9
    - Solubility : Sparingly soluble in water but swells in water forming
    a viscous solution

❖ **Storage condition**

    Store in dry and cool place

❖ **Uses**

    - Used as a gelling agent in the formulation of gels.
    - Used as a binder at low concentrations in the preparation of tablets.
    - Used as release retardant polymer in both sustained and controlled release
    tablet formulations at high concentrations
    - Also acts a disintegrant in immediate release tablet formulations at very
    low concentrations.
2.15. LITERATURE ON ANACARDIUM OCCIDENTALE TREE GUM (50-53)

❖ **Common name**

Cashew gum

❖ **Taxonomy**

- Phylum: Magnoliophyta
- Class: Magnoliopsida
- Order: Sapindales
- Family: Anacardiaceae
- Genus: Anacardium

❖ **Description**

Pale pink to half white coloured fine amorphous powder

❖ **Composition**

Cashew gum is chemically composed of 61 % galactose, 14 % arabinose, 7 % rhamnose, 8 % glucose, 5 % glucuronic acid and < 2 % other sugar residues, while hydrolysis of the gum yields L-arabinose, L-rhamnose, D-galactose and glucuronic acid. The gum has a highly branched galactan framework comprising of chains of (1→3) linked β-D galactopyranosyl units interspersed with β(1→6) linkages. The purified gum also contains traces of iron, magnesium, calcium.

❖ **Ash values for % w/v cashew gum**

- Water soluble value: 0.76 ± 0.03
- Alcohol value: 0.09 ± 0.01
- Water soluble ash value: 0.76 ± 0.03
- Acid insoluble ash value: 0.09 ± 0.03
- Total ash: 0.75 ± 0.03

❖ **Storage**

Store in a dry and cool place without moisture

❖ **Uses**

- Used as gelling agent for the preparation of gels.
- The mucilage is used as a binder for the formulation of tablets.
- The finely powdered gum is used as a release rate retardant polymer for the preparation of both controlled and sustained release tablet formulations.
2.16. LITERATURE ON DELONIX REGIA SEED ENDSPERM GUM (54-56)

❖ Synonym
   *Poinciana regia*

❖ Common names
   Flamboyant gum, Gulmohar seed gum, Flamtree gum

❖ Taxonomy
   - Class : Equisetopsida
   - Subclass : Magnoliidae
   - Order : Fabales
   - Family : Leguminosae/Fabaceae – Caesalpinioideae
   - Genus : Delonix

❖ Description
   Pale yellow coloured fine amorphous powder, odourless and hygroscopic.

❖ Composition
   The few branch regions in flamboyant seed gum consist of a-D-mannose (1-4) linkages and a-D-galactose (1-6) branches (mannose–galactose 2:1 ratio). Its mannose and galactose proportions are similar to those of guar gum but differ in terms of the OH bond position in the main chain: flamboyant gum (FNG) has a-D-mannose while the guar gum has b-D-mannose.

❖ Storage conditions
   Stored in a dry place at 25 °C

❖ Relative solubility:
   Slowly soluble in cold water quickly soluble in hot water; form a viscous colloidal solution. Practically insoluble in organic solvents.

❖ Uses
   - Mainly used as the release rate retarding polymer in controlled/sustained release tablet formulation at high concentrations and also used as a binder at low concentrations.
   - Used as a suspending agent in suspensions & as a polymer in micro beads.
2.17. LITERATURE ON ETHYL CELLULOSE (N22, N50 & N100) (83)

- **Non-proprietary Names**
  
  Ethyl Cellulose (BP; JP; PhEur & USP-NF)

- **Synonyms**
  
  Aqua coat ECD, Aqualon, Ethocel, Surelease.

- **Chemical structure**

  ![Chemical structure of Ethyl cellulose](image)

  **Figure 2.4: Chemical structure of Ethyl cellulose**

- **Chemical Name, Empirical Formula**
  
  Cellulose ethyl ether; \([C_6H_7O_2 (OC_2H_5)_3]_n\)

- **Molecular weight**
  
  Ethyl cellulose with complete ethoxyl substitution (DS = 3) is \(C_{12}H_{23}O_6\) \((C_{12}H_{22}O_5) \)\( C_{12}H_{23}O_5\) where \(n\) can vary to provide a wide variety of molecular weights. Ethyl cellulose, an ethyl ether of cellulose, is a long-chain polymer of \(\beta\)-anhydroglucose units joined together by acetyl linkages.

- **Description**
  
  Ethyl cellulose is a tasteless, free flowing, white to light tan colored powder.

- **Solubility**

  - Practically insoluble in glycerin, water and propylene glycol.
  - Soluble in acetone, esters, aromatic hydrocarbons, alcohols and ketones.
  - Freely soluble in chloroform, methyl acetate and tetrahydrofuran and in mixtures of aromatic hydrocarbons with ethanol (95%).

- **Properties**

  - **Melting point**: 160 – 210 °C.
  - **Density**: 0.4g/cm³ (bulk)
  - **Moisture content**: Absorbs very little water from the humid air or during.
• **Viscosity**: The viscosity of ethyl cellulose is measured typically at 25°C using 5% w/v ethyl cellulose dissolved in a solvent blend of 80% toluene: 20% ethanol (w/w).
  - Ethyl cellulose N-22 – 18-24 mPas
  - Ethyl cellulose N-50 – 40-52 mPas
  - Ethyl cellulose N-100 – 80-105 mPas

❖ **Functional category**

  The coating agent, flavoring fixative, tablet binder, tablet filler, viscosity increasing agent.

❖ **Applications in Pharmaceutical formulations**

  • As tablet adhesive and thin film coating material.
  • In oral formulations, as a hydrophobic coating agent for tablets and granules.
  • Coatings are used to modify the release of a drug, to mask an unpleasant taste, or to improve the stability of a formulation.
  • Modified release tablet formulations may also be produced using ethyl cellulose as a matrix former.
  • Ethyl cellulose, dissolved in an organic solvent or solvent mixture, can be used on its own to produce water-insoluble films. Higher-viscosity ethyl cellulose grades tend to produce stronger and more durable films.
  • In topical formulations, used as a thickening agent in creams, lotions, or gels, provided an appropriate solvent is used.
  • As a stabilizer for emulsions.
  • Used in cosmetics and food products.
  • High-viscosity grades of ethyl cellulose are used in drug microencapsulation

❖ **Stability and storage conditions**

  Ethyl cellulose is stable, slightly hygroscopic material. Chemically resistant to alkalis, both dilute and concentrated and to salt solutions.

❖ **Safety**

  Widely used in oral and topical pharmaceutical formulations. Because ethyl cellulose is not metabolized it is not recommended for parenteral products.
2.18. LITERATURE ON EUDRAGIT (RLPO & RS PO)\(^{(83)}\)

- **Synonyms**
  Polymeric methacrylates; Polymethacrylates

- **Chemical structure**

![Chemical structure of Eudragit](image)

_Figure 2.5: Chemical structure of Eudragit_

For RL & RS: \(R^1 = H, CH_3\); \(R^2 = CH_3, C_2H_5\); \(R^3 = CH_3\)

- **Chemical name**
  Poly (ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) [For RLPO – 1:2:0.2 & RSPO – 1:2:0.1]

- **Description**
  - Typically, the molecular weight of these polymers is >100000
  - Fine, white powders with a slight amine-like odor. They are characteristically the same polymers and differ in permeability.
  - Eudragit RL and Eudragit RS, are copolymers synthesized from acrylic acid and methacrylic acid esters, with Eudragit RL (Type A) having 10% of functional quaternary ammonium groups and Eudragit RS (Type B) having 5% of functional quaternary ammonium groups. The ammonium groups are present as salts and give rise to the pH-independent permeability of the polymers. Both polymers are water-insoluble, and films prepared from Eudragit RL are freely permeable to water, whereas, films prepared from Eudragit RS are only slightly permeable to water.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Form</th>
<th>Dry weight</th>
<th>Solvent</th>
<th>Permeability</th>
<th>Viscosity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSPO</td>
<td>Powder</td>
<td>≥97%</td>
<td>Acetone, Alcohols</td>
<td>Low</td>
<td>≤5 mPas</td>
</tr>
<tr>
<td>RLPO</td>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td></td>
</tr>
</tbody>
</table>
Solubility
- 1 g of the substance dissolved in 7 g aqueous methanol, ethanol and isopropyl alcohol (containing approx. 3 % water), as well as in acetone.
- Ethyl acetate and methylene chloride to give clear to cloudy solutions.
- The substances are practically insoluble in petroleum ether, 1N sodium hydroxide and water.

Specifications
- Loss on drying : ≤3.0%
- Heavy metals : ≤20ppm

Functional category
- Film former; tablet binder; tablet diluents.

Applications in Pharmaceutical formulations
- Primarily used in oral capsule and tablet formulations as film-coating agent to form water-insoluble film coats for sustained-release products
- Also used as binders in both aqueous and organic wet granulation processes.
- Larger quantities (5–20%) of the dry polymer are used to control the release of an active substance from a tablet matrix.
- Solid polymers may be used in direct compression processes in quantities of 10–50%.
- Additionally used to form the matrix layers of transdermal delivery systems and have also been used to prepare novel gel formulations for rectal administration.

Stability and storage conditions
- Dry powders are stable for at least 3 years if stored in a tightly closed container at less than 30 °C.
- Powders tend to form clumps, although this does not affect the quality of the substance and the clumps can readily be broken up.

Safety
- Regarded as Non-toxic, and Non-irritant material.
- Widely used as film coating materials in oral pharmaceutical formulations.
2.19. LITERATURE ON HYDROXYETHYL CELLULOSE (83)

❖ Non-proprietary Names

Hydroxy Ethyl Cellulose (BP, PhEur & USP-NF)

❖ Synonyms

Cellosize HEC, Hyetellose, Cellulose hydroxyethyl ether, HEC, HE Cellulose

❖ Chemical structure

![Chemical structure of hydroxyethyl cellulose](image)

R is H or $[-\text{CH}_2\text{CH}_2\text{O}-]_m\text{H}$; where m is a common integral number

**Figure 2.6: Chemical structure of hydroxyethyl cellulose**

❖ Viscosity

- Hydroxyethyl cellulose is available in a wide range of viscosity types; e.g. Cellosize is manufactured in 11 regular viscosity grades. Hydroxyethyl cellulose grades differ principally in their aqueous solution viscosities which range from 2–20,000 mPas for a 2% w/v aqueous solution.
- Two types of Cellosize are produced, a WP-type, which is a normal dissolving material, and a QP-type, which is a rapid-dispersing material.
- The lowest viscosity grade (02) is available only in the WP type. Five viscosity grades (09, 3, 40, 300, and 4400) are produced in both WP- and QP-types. Five high-viscosity grades (10000, 15000, 30000, 52000, and 100M) are produced only in the QP-type.
- The viscosity of 5% w/v of WP type 3 grade at 25 °C is 285-350 mPas.

❖ Applications in Pharmaceutical formulations:

- Used as a thickening agent in ophthalmic and topical formulations.
- Also used as a binder and film-coating agent for tablets.
- It is present in lubricant preparations for dry eye, contact lens care.
- The concentration of hydroxyethyl cellulose used in a formulation is dependent upon the solvent and the molecular weight of the grade.
- Also widely used in cosmetics.
2.20. LITERATURE ON HYPROMELLOSE (E15; E5) (83)

❖ Non-proprietary Names:
   Hypromellose (BP); Hydroxypropyl methylcellulose (USP-NF)

❖ Synonym
   E464; HPMC; Methocel; Metolose; Pharmacoat;

❖ Chemical structure

![Chemical structure of HPMC](image)

where R is H, CH₃ or [CH₃CH (OH)CH₂]

Figure 2.7: Chemical structure of HPMC

❖ Viscosity

Viscosity values for 2% (w/v) aqueous solutions of Methocel at 20 °C
Methocel E5 – 5 mPas and Methocel E15 – 15 mPas

❖ Application in Pharmaceutical Formulation or Technology:

- Hypromellose is widely used in oral and topical pharmaceutical formulations.
- In oral products, hypromellose is primarily used as a tablet binder, in film coating and as an extended-release tablet matrix.
- Depending upon the viscosity grade, the concentration of 2-20% w/w is used for film-forming solutions to film coat tablets. Lower-viscosity grades are used in aqueous film-coating solutions while higher viscosity grades are used with organic solvents.
- Hypromellose at a concentration between 0.45-1.0% w/w may be added as a thickening agent to vehicles for eye drops and artificial tear solution.
- Used as an emulsifier, suspending agent, and stabilizing agent in topical gels and ointments.
2.21. LITERATURE ON SODIUM STARCH GLYCOLATE

🔹 Non-proprietary names
Sodium starch glycolate (BP; PhEur; USP-NF)

🔹 Synonyms
Carboxymethyl Starch (Sodium salt), Explotab, Primojel.

🔹 Chemical structure

![Chemical structure of Sodium starch glycolate](image)

Figure 2.8: Chemical structure of Sodium starch glycolate

🔹 Chemical name
Sodium carboxymethyl starch

🔹 Description
Sodium starch glycolate is the sodium salt of a carboxymethyl ether of starch. Very fine, white or off-white, free-flowing powder, odorless or almost odorless.

🔹 Functional category:
As a disintegrant in capsule and tablet formulations.

🔹 Applications in Pharmaceutical Formulation or Technology
- As disintegrant in capsule and tablet formulations and commonly used in tablets prepared by either direct compression or wet granulation processes.
- The usual concentration employed in a formulation is between 2% and 8%, with the optimum concentration about 4%, and in many cases 2% is sufficient.

🔹 Solubility
Partially insoluble in water and insoluble in organic solvents. It gives a translucent suspension in water.

🔹 Stability and storage condition
A tablet prepared with sodium starch glycolate have good storage properties. Sodium starch glycolate is stable and should be stored in a well-closed container to protect it from wide variation in humidity and temperature that may cause caking.
2.22. LITERATURE ON POLYVINYL PYRROLIDONE K30 (83)

❖ Synonyms
E1201; Kollidon; Plasdone; polyvidone; polyvinyl pyrrolidone; povidonum; Povipharma; PVP; 1-vinyl-2-pyrrolidinone polymer.

❖ Chemical Name, Empirical Formula and Molecular Weight
1-Ethenyl-2-pyrrolidinone homopolymer; (C₆H₉NO)n and 50,000

❖ Description
Povidone occurs as a fine, white to creamy-white colored, odourless or almost odorless, hygroscopic powder. Povidones with K-values equal to or lower than 30 are manufactured by spray-drying and occur as spheres.

❖ Applications in Pharmaceutical Formulation or Technology
- In tableting, povidone solutions are used as binders in wet granulation processes.
- Povidone is also added to powder blends in the dry form and granulated in situ by the addition of water, alcohol, or hydroalcoholic solutions.
- The solubility of a number of poorly soluble active drugs may be increased by mixing with povidone.

2.23. LITERATURE ON MICROCRYSTALLINE CELLULOSE (83)

❖ Synonyms
Avicel pH, Cellulose gel, Avicel CL-611; Avicel RC-501; Avicel RC-581; Avicel RC-591; Avicel RC/CL

❖ Description
Microcrystalline cellulose is purified partially polymerised cellulose that occurs as a white, odourless, tasteless, crystalline powder composed of porous particles.

❖ Applications in Pharmaceutical Technology
- Microcrystalline cellulose is widely used in pharmaceuticals primarily as a binder/diluents in oral tablet and capsule formulations.
- Microcrystalline cellulose also has some lubricant and disintegrant properties that makes it useful in tableting.
2.24. LITERATURE ON STARCH (83)

❖ Synonyms
   Aytex P; Instant Pure-Cote; Pure-Bind: Tablet White; Fluxtex W; Melogel.

❖ Description
   Starch occurs as an odorless and tasteless, fine, white colored powder comprising very small special or ovoid granules whose size and shape are characteristics for each botanical variety.

❖ Applications in pharmaceutical formulation or technology
   • Starch is used as an excipient primarily in oral solid-Dosage Formulations where it is utilized as a binder, diluent, and disintegrant.
   • In Tablet formulations freshly prepared starch paste is used at a concentration of 5-25%/w/w in tablet granulations as a binder.
   • Starch is one of the most commonly used tablet disintegrant at concentrations of 3-15%/w/w.
   • Starch is used in topical preparation such as dusting powders for its absorbency and as a protective covering in ointment formulations applied to the skin.

2.25. LITERATURE ON LACTOSE, ANHYDROUS (83)

❖ Synonyms
   Anhydrous lactose NF; Lactosum; Milk sugar; Saccharum lactis.

❖ Chemical name, Empirical formula and Molecular weight
   O-β-D-galactopyranosy-(1-4)-β-D-glucopyranose; C₁₂H₂₂O₁₁ & 342.30

❖ Description
   Lactose occurs as white to off-white crystalline particles or powder. Several different brands of anhydrous lactose are commercially available which contain anhydrous B lactose and anhydrous lactose.

❖ Applications in Pharmaceutical Formulation or Technology
   • Widely used in direct compression tableting applications.
   • Used as a tablet and capsule filler and binder.
   • Used with moisture sensitive drugs due to its low moisture content.
2.26. LITERATURE ON TALC \(^{(83)}\)

- **Synonyms**
  - Hydrous magnesium calcium silicate; Hydrous magnesium silicate; Steatite.
- **Chemical name, Empirical formula and Molecular weight**
  - Talc; Talc is a purified, hydrated, magnesium silicate, approximating to the formula \(\text{Mg}_6(\text{SiO}_5)_4(\text{OH})_4\). It may contain small, variable amounts of aluminum silicate and iron.
- **Applications in Pharmaceutical Formulation or Technology**
  - Widely used in oral solid dosage formulations as a lubricant and diluents.
  - As a dissolution retardant in the development of controlled-release products.
  - As a lubricant in tablet formulations in a novel powder coating for extended-release pellets and as an adsorbent.
  - In topical preparations, talc is used as a dusting powder, although it should not be used to dust surgical gloves.
  - Talc is a natural material; it may contain microorganisms and should be sterilized when used as a dusting powder.
  - Talc is used to clarify liquids and is also used in cosmetics and food products, mainly for its lubricant properties.

2.27. LITERATURE ON MAGNESIUM STERATE \(^{(83)}\)

- **Synonyms**
  - Magnesium octadecanoic acid, Magnesium salt.
- **Chemical name, Empirical formula and Molecular weight**
  - Octadecanoic acid magnesium salt; \(\text{C}_{36}\text{H}_{70}\text{MgO}_4\ & & 591.34\). The USPNF 23 describes magnesium stearate as a compound of magnesium with a mixture of solid organic acids that consists chiefly of variable proportions of magnesium stearate and magnesium palmitate (\(\text{C}_{32}\text{H}_{62}\text{MgO}_4\)).
- **Applications in Pharmaceutical Formulation or Technology**
  - Widely used in cosmetics, foods, and pharmaceutical formulations.
  - It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25% and 5.0%w/w.
  - It is also used in barrier creams.