DRUG AND POLYMER PROFILES

4.1 MATERIALS

Table 4.1: Drugs Used In the Current Study

<table>
<thead>
<tr>
<th>Name of the drug</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ofloxacin</td>
<td>Ranbaxy Laboratories Limited</td>
</tr>
<tr>
<td>Glipizide</td>
<td>RPG Life sciences</td>
</tr>
</tbody>
</table>

Table 4.2: Excipients and Chemicals used in Current Study

<table>
<thead>
<tr>
<th>Name of the Chemicals / Excipients</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyvinylpyrrolidone K30</td>
<td>Loba Chemie Pvt. Ltd., Mumbai</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>S.D. Fine Chemicals Ltd., Mumbai</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>S.D. Fine Chemicals Ltd., Mumbai</td>
</tr>
<tr>
<td>Dicalcium phosphate</td>
<td>Shreeji Pharma Pvt Ltd</td>
</tr>
<tr>
<td>Lactose</td>
<td>Shreeji Pharma Pvt Ltd</td>
</tr>
<tr>
<td>Iso Propyl Alcohol</td>
<td>Fischer scientific Ltd</td>
</tr>
<tr>
<td>Acetonitrile (HPLC Grade)</td>
<td>Merck, India</td>
</tr>
<tr>
<td>Methanol (HPLC Grade)</td>
<td>Merck, India</td>
</tr>
<tr>
<td>Water (HPLC Grade)</td>
<td>Merck, India</td>
</tr>
<tr>
<td>Name of the Equipment</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>Brookfield cone and plate viscometer (LV DV-III+)</td>
<td>Brookfield engineering laboratories</td>
</tr>
<tr>
<td>Tablet compression machine(10 station)</td>
<td>Cadmach Machinery Co</td>
</tr>
<tr>
<td>Electronic balance</td>
<td>Shimadzu</td>
</tr>
<tr>
<td>pH meter(Model no.361)</td>
<td>Systronics</td>
</tr>
<tr>
<td>Karl Fischer Auto Titrator(Model no.349)</td>
<td>Systronics</td>
</tr>
<tr>
<td>Bulk density apparatus</td>
<td>Electrolab</td>
</tr>
<tr>
<td>UV visible spectrophotometer</td>
<td>Shimadzu</td>
</tr>
<tr>
<td>Hardness tester(MHT-20)</td>
<td>Campbell Electronics</td>
</tr>
<tr>
<td>Friability tester (FTA-20)</td>
<td>Campbell Electronics</td>
</tr>
<tr>
<td>Dissolution apparatus(DISSO-2000)</td>
<td>Labindia</td>
</tr>
<tr>
<td>IR(Model no. 841)</td>
<td>Perkin-Elmer</td>
</tr>
<tr>
<td>DSC(DSC-50)</td>
<td>Shimadzu</td>
</tr>
<tr>
<td>Stability chambers</td>
<td>Thermolab Scientific Equipments Pvt Ltd</td>
</tr>
<tr>
<td>Sonicator (Power sonic 505)</td>
<td>PCI analyticals Pvt Ltd.</td>
</tr>
<tr>
<td>HPLC(- LC UV-100)</td>
<td>Cyberlab</td>
</tr>
<tr>
<td>Microcentrifuge</td>
<td>Remi Equipment</td>
</tr>
</tbody>
</table>
4.2 DRUG PROFILES

4.2.1 OFLOXACIN

Physicochemical properties

i) Description: Pale yellowish white to light yellowish white crystals or crystalline powder

ii) Molecular formula: $C_{18}H_{20}FN_3O_4$

iii) Molecular weight: 361.4

iv) Chemical name $^{70,71}$: (±)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H pyrido [1,2,3-de]-1,4-benzoxazine-6-carboxylic acid

v) Chemical structure:

![Chemical structure of Ofloxacin](image)

vi) Solubility: Slightly soluble in water, alcohol, methanol and dichloro methane. Sparingly soluble in glacial acetic acid.

vii) Partition coefficient (log P): 0.33

viii) pH solubility: Highly soluble in range of 2-5 and poorly soluble from 5-8.
**Mechanism of action:** Ofloxacin is a fluoroquinolone antibacterial which acts by inhibiting the A subunit of DNA gyrase (topoisomerase) which is essential in the reproduction of the bacterial DNA.

**Pharmacokinetics:** Ofloxacin is rapidly and well absorbed from the GIT. Oral bioavailability is almost 100% and a peak plasma concentration of 3 to 5 mcg/ml is achieved 1 to 2 hours after a dose of 400 mg by mouth. Absorption may be delayed by the presence of food, but the extent of absorption is not substantially affected. The plasma half life ranges from 4 to 7 hours and in renal impairment values of 15 to 60 hours have been reported. About 25% is bound to plasma proteins. It is widely distributed in body fluids, including CSF and the tissue penetration is also good.

It crosses the placenta and is distributed into the breast milk. It also appears in the bile. There is limited metabolism to desmethyl and n-oxide derivatives. Ofloxacin is mainly eliminated by the kidneys. Excretion is by tubular secretion and glomerular filtration. 65 to 80% of a dose is excreted unchanged in the urine over 24 to 48 hours, resulting in high urinary concentrations. Less than 5% is excreted in the urine as metabolites. 4 to 8% of the dose may be excreted in the faeces. Small amounts are also removed by hemodialysis.

**Uses:** Ofloxacin is a fluoroquinolone antibacterial used similar to ciprofloxacin and has a wide spectrum of activity than nalidixic acid. It has been used in the treatment of infections including biliary tract infection, anthrax, infected bites and stings, bone and joint infections, chanchroid, exacerbations of cystic fibrosis, gastroenteritis, gonorrhea, infections in immune compromised patients (neutropenia), otitis externa, otitis media, peritonitis, fever, lower respiratory tract infections, septicemia, spotted fever, skin infections, typhoid, typhus and urinary tract infections.
It is also used in the treatment of Chlamydia or chlamydiophilia infections including non-gonococcal urethritis and in mycobacterial infections such as leprosy.

**Dosage and Administration:** Ofloxacin is given by mouth as a base or intravenously as the hydrochloride. The oral or IV dose ranges from 200mg daily to 400mg twice daily depending on the severity and nature of the infection. Oral dose up to 400mg may be given as a single dose, preferably in the morning.

### 4.2.2 GLIPIZIDE

**Physicochemical properties**

i) Description: Glipizide is a whitish, odorless powder

ii) Molecular Formula: C$_{21}$H$_{27}$N$_{5}$O$_{4}$S

iii) Molecular weight: 445.536 g/mol

iv) Chemical name: N-(4-[N-(cyclohexylcarbamoyl) sulfamoyl]phenethyl)-5-methylpyrazine-2-carboxamide

v) Chemical structure:
vi) Solubility: It is insoluble in water and alcohols, but soluble in 0.1 N NaOH; it is freely soluble in dimethylformamide.

vii) pH solubility: Soluble in 0.1N HCl

**Mechanism of action:** Glipizide appears to lower blood glucose acutely by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells in the pancreatic islets. Extrapancreatic effects also may play a part in the mechanism of action of oral sulfonylurea hypoglycemic drugs.

**Pharmacokinetics**\(^{72}\): Glipizide is rapidly absorbed with a time to maximum plasma level of about 2 hours. Distributed into the liver and blood, with lower concentrations in the lungs, kidneys and very small amounts are distributed into erythrocytes and saliva. Appears to be almost completely metabolized, mainly in the liver. Glipizide and its metabolites are excreted principally in urine (60–90%) and to a lesser extent in feces.

**4.2.2.4 USES:** Lowers blood glucose concentration in diabetic and nondiabetic individuals. Stimulates secretion of postprandial endogenous insulin from the beta cells of the pancreas.

**4.3 EXCIPIENT PROFILES**

**4.3.1 Magnesium stearate**\(^{73}\)

a) **Synonyms:** Dibasic magnesium stearate, magnesium distearate, magnesia stearas, magnesium octa decanoate.

b) **Chemical name:** Octadecanoic acid magnesium salt

c) **Empirical formula:** \(C_{36}H_{70}MgO_4\)

d) **Molecular weight:** 591.24
e) **Description:** Magnesium stearate is a very fine, light white, precipitated or milled, impalpable powder of low bulk density, having a faint odor of stearic acid and a characteristic taste. The powder is greasy to the touch and readily adheres to the skin.

f) **Melting range:** 117–150°C

g) **Stability and storage conditions:** Magnesium stearate is stable and should be stored in a well-closed container in a cool, dry place

h) **Applications:** Magnesium stearate is 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.

4.3.2 Sodium bicarbonate

a) **Synonyms:** Baking soda, E500, Effer-Soda, monosodium carbonate, sodium acid carbonate, sodium hydrogen carbonate.

b) **Chemical name:** Carbonic acid monosodium salt

c) **Empirical formula:** NaHCO₃

d) **Molecular weight:** 84.01

e) **Description:** Sodium bicarbonate occurs as an odorless, white, crystalline powder with a saline, slightly alkaline taste. The crystal structure is monoclinic prisms. Grades with different particle sizes, from a fine powder to free-flowing uniform granules, are commercially available.

f) **Melting point:** 270°C

g) **Stability and storage conditions:** When heated to about 50°C, sodium bicarbonate begins to dissociate into carbon dioxide, sodium carbonate, and water; on heating to 250 to 300°C, for a short time, sodium bicarbonate is completely converted into anhydrous sodium carbonate.
h) **Applications:** Sodium bicarbonate is generally used in pharmaceutical formulations as a source of carbon dioxide in effervescent tablets and granules. It is also widely used to produce or maintain an alkaline pH in a preparation. In effervescent tablets and granules, sodium bicarbonate is usually formulated with citric and/or tartaric acid\(^\text{116}\); combinations of citric and tartaric acid are often preferred in formulations as citric acid alone produces a sticky mixture that is difficult to granulate, while if tartaric acid is used alone, granules lose firmness.

**4.3.3 Dibasic calcium phosphate\(^\text{75}\)**

a) **Synonyms:** Calcium monohydrogen phosphate; calcium orthophosphate; Di-Cafos AN; dicalcium orthophosphate;

b) **Chemical name:** Dibasic calcium phosphate

c) **Empirical formula:** CaHPO\(_4\)

d) **Molecular weight:** 136.06

e) **Description:** Anhydrous dibasic calcium phosphate is a white, odorless, tasteless powder or crystalline solid. It occurs as triclinic crystals.

f) **Melting range:** does not melt; decomposes to form calcium pyrophosphate.

g) **Stability and storage conditions:** Dibasic calcium phosphate is a nonhygroscopic, relatively stable material. Under conditions of high humidity it does not hydrate to form the dihydrate. The bulk material should be stored in a well-closed container in a dry place.

h) **Applications:** Dibasic calcium phosphate is used both as an excipient and as a source of calcium in nutritional supplements. It is used particularly in the nutritional/health food sectors. It is also used in pharmaceutical products because of its compaction properties, and the good flow properties of the coarse-grade material.
4.3.4 Xanthan gum

a) **Synonyms:** Corn sugar gum; Keltrol;

b) **Chemical name:** Xanthan gum

c) **Empirical formula:** \((C_{35}H_{49}O_{29})_n\)

d) **Molecular weight:** Approximately \(2 \times 10^6\)

e) **Description:** Xanthan gum occurs as a cream- or white-colored, odorless, free-flowing, fine powder.

f) **Functional category:** Stabilizing agent; suspending agent; viscosity-increasing agent.

g) **Stability and storage conditions:** Xanthan gum is a stable material. Aqueous solutions are stable over a wide pH range (pH 3–12), although they demonstrate maximum stability at pH 4–10 and temperatures of 10–60°C.

h) **Applications:** Xanthan gum is widely used in oral and topical pharmaceutical formulations, cosmetics, and foods as a suspending and stabilizing agent. It is also used as a thickening and emulsifying agent.

4.3.5 Lactose

a) **Synonyms:** lactosum; lattioso; milk sugar; Pharmatose DCL 21;

b) **Chemical name:** \(O-\beta-D\text{-galactopyranosyl-(1\rightarrow4)}-\beta-D\text{-glucopyranose}\)

c) **Empirical formula:** \(C_{12}H_{22}O_{11}\)

d) **Molecular weight:** 342.30

e) **Description:** Lactose occurs as white to off-white crystalline particles or powder. Several different brands of anhydrous lactose are commercially available which contain anhydrous \(\beta\)-lactose and anhydrous \(\alpha\)-lactose.

f) **Melting range:** \(223.0^\circ C\) for anhydrous \(\alpha\)-lactose; \(252.2^\circ C\) for anhydrous \(\beta\)-lactose;
g) **Stability and storage conditions:** Mold growth may occur under humid conditions (80% RH and above). Lactose may develop a brown coloration on storage, the reaction being accelerated by warm, damp conditions;

h) **Applications:** lactose is widely used in direct compression tabletting applications and as a tablet and capsule filler and binder.

4.3.6 Povidone

a) **Description:** Povidone occurs as a fine, white to creamy-white colored, odorless or almost odorless, hygroscopic powder. Povidones with K-values equal to or lower than 30 are manufactured by spray-drying and occur as spheres. Povidone K-90 and higher K-value povidones are manufactured by drum drying and occur as plates.

b) **Empirical Formula:** (C₆H₉NO)ₙ

c) **Molecular Weight:** 2500–3 000 000.

   It is characterized by its viscosity in aqueous solution, relative to that of water, expressed as a K-value, in the range 10–120.

d) **pH (5% w/v aqueous solution):** 3.0–7.0

e) **Moisture content:** Povidone is very hygroscopic with significant amounts of moisture being absorbed at low relative humidities.

f) **Solubility:** It is freely soluble in acids, chloroform, ethanol (95%), ketones, methanol, and water; practically insoluble in ether, hydrocarbons, and mineral oil. In water, the concentration of a solution is limited only by the viscosity of the resulting solution, which is a function of the K-value.
g) **Functional Category:** Disintegrant; dissolution aid; suspending agent; tablet binder.

h) **Applications:** In tabletting, 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 hydro alcoholic solutions. Povidone is used as a solubilizer in oral and parenteral formulations and has been shown to enhance dissolution of poorly soluble drugs from solid-dosage forms. Povidone solutions may also be used as coating agents. Povidone is additionally used as a suspending, stabilizing, or viscosity-increasing agent in a number of topical and oral suspensions and solutions. The solubility of a number of poorly soluble active drugs may be increased by mixing with povidone.