CHAPTER - 4

DRUG AND EXCIPIENT PROFILE
4. DRUG AND EXCIPIENT PROFILE

4.1 Piroxicam

**Description:** Piroxicam belongs under nonsteroidal anti-inflammatory drug. Piroxicam is of oxicam class. It is a Cox-1 (Cyclooxygenase) inhibitor. Colour of piroxicam is white. Piroxicam is crystalline in nature. Piroxicam is sparingly soluble in water, dilute acid and organic solvents whereas it is slightly soluble in alcohols (www.everydayhealth.com › Drugs › Nonsteroidal Anti-Inflammatory Agents.)

**IUPAC name:** 4-Hydroxy-2-methyl-N-(2-pyridyl)-2H-1,2-benzothiazin-3-caboxamid-1,1-dioxid. (https://www.drugbank.ca/drugs/DB00554)

**Chemical Structure:**

![Chemical structure of piroxicam](image)

**Figure 7:** Chemical structure of piroxicam

**CAS Registry number:** 36322-90-4

**Molecular weight:** 331.35

**Melting point:** 240 - 245 °C

**Solubility:** sparingly soluble in water.

**Partition coefficient (Log P):** 3.1

**Drug category:** Non-steroidal anti-inflammatory agents
**Indication:** Piroxicam is indicated in the treatment of inflammatory disorders like rheumatoid arthritis, gout, bursitis, menstruation and headache.

**Pharmacology:**

**Mechanism of action** - Piroxicam inhibits cyclooxygenases (nonselective), which produces prostaglandins. Piroxicam antagonizes COX by binding to the upper portion of the active site and preventing its substrate, arachidonic acid, from entering the active site. It also prevents migration of leukocytes into area of swelling and inhibits thromboxane A2 production by the platelets.

**Pharmacokinetics:**

**Absorption** - By oral or rectal route.

Distribution-The $V_d$ is approximately 0.14 L/kg.

**Metabolism**- Metabolism occurs by hydroxylation at pyridyl side chain, by cyclodehydration, hydrolysis of the amide linkage, decarboxylation, and N-demethylation.

**Excretion**- Piroxicam get excreted by urine and feces and also in breast milk.

**Half-life:** Plasma half-life about 30 to 60 hours.

**Adverse Reactions:**

**Cardiovascular**- It causes edema, alterations in blood pressure, dilation of vessels, palpitations, tachycardia.

**CNS**-It causes headache, dizziness, vertigo, depression, insomnia, nervousness.

**Dermatologic**- Pruritus, sweating, erythema. (https://en.wikipedia.org/wiki/Piroxicam.)

**EENT**-Tinnitus, swollen eyes, blurred vision.

**GI**- Epigastric distress, vomiting, constipation and anorexia.

**Genitourinary**-Hematuria, proteinuria, increased serum creatinine, acute renal insufficiency and failure.
**Hematologic**- Increased bleeding time, thrombocytopenia.

**Hepatic**- Elevated liver enzymes.

**Respiratory**- Dyspnea, shortness of breath.

**Storage:** Stored at room temperature.

**Dose:** 20 mg daily or 10 mg two times a day with food.

(https://www.drugs.com/cdi/piroxicam.html.)

### 4.2 Excipients profile

All the excipients used in present research work are commonly used excipients in industrial practice. All excipients can be handled without any special needs and precautions unless otherwise mentioned. They were not having issues about handling, safety, incompatibility and storage conditions. All materials were non-toxic, non-irritant and non-inflammable and were used within specified *Industrial Insulation Group* limit as per US-FDA recommendations.

#### 4.2.1 Hydroxy propyl methyl cellulose (HPMC)

**Synonyms:** Metolose, Methocel, Pharmacoat, Beneceletc.

**Description:** Hydroxypropyl methylcellulose has noodour and taste and appears white or creamy white. Nature of Hydroxypropyl methylcellulose is fibrous or granular powder.

**Structural formula:** Where R is CH3, H or Isopropyl alcohol group.

![Figure 8: Structure of hydroxy propyl methyl cellulose](image-url)
Category: Coating agent for tablet, film forming agent, control release polymer, binding agent and viscosity increasing agent.

Applications:

In oral products:

- 2-5% of concentration used as a binding agent for tablet.
- High viscosity grades HPMC in 10-80% concentration used as control release polymer.
- 2-20% is used as film former.

In topical products:

- 0.45-1.0% of concentration used as a viscosity increasing agent.

Typical properties:

pH: 5.5-8.0 for a 1% aqueous solution.

Ash: 1.5-3.0%.

Melting point: 190-200ºC.

Moisture content: It absorbs moisture.

Solubility: Soluble in cold water. (Owen, 2006 and Rowe, 1980)

4.2.2 Hydroxy propyl cellulose

Synonyms: 2-hydroxypropyl ether (low-substituted) cellulose, L-HPC, oxypropylated cellulose.

Chemical name: Cellulose, 2-hydroxypropyl ether.

Description: L-HPC is tasteless, odorless or with slight odor white to yellowish white powder or granules.
Structural formula:

\[
R \text{ is } H \text{ or } [\text{CH}_2\text{CH(\text{CH}_3)O}]_m \text{ H}
\]

Figure 9: Chemical structure of low substituted hydroxy propyl cellulose

**Functional category:** Disintegrate (disintegrating agent), binder.

**Applications:** It is primarily used as a disintegrating agent and as a binder for tablets in 5–50% concentration.

**Typical properties:**

\( \text{pH} \): 5.0–7.5 for 1%.

**Density:** 1.3 g/cm\(^3\).

**Melting point:** 290°C.

**Solubility:** Insoluble in water, 95% ethyl alcohol and ether.

**Storage:** Stored in a well-closed container.

**LD\text{so} (rat, oral):** >15 g/kg. (Banker et al., 1981)

4.2.3 Neusilin US2

Neusilin US 2 is a synthetic, amorphous powder with multifunctional capacity. Neusilin US 2 is mostly used for enhancement of quality of tablets, powder, granules and capsules.
Empirical formula: \( \text{Al}_2\text{O}_3\cdot\text{MgO} \cdot 1.7\text{SiO}_2 \cdot x\text{H}_2\text{O} \).

**Characteristics:**

- It occurs as a fine powder or as granules of magnesium aluminometasilicate.
- It possesses large specific surface area.
- It has high oil adsorption capacity.
- It has water adsorption capacity.
- It has a long shelf life.

**Application of neusilin US2:** It is used in formulation of SNEDDS and solid dispersion, diluent, binder, disintegrating agent, anticaking agent and used in solidification of liquid API.

**General properties of neusilin US2:**

**Appearance:** White granules.

**Physical form:** Amorphous.

**True specific gravity:** 2.0-2.2

**Solubility:** Practically in soluble in ethanol.

**Composition (%) on dried basis:** \( \text{Al}_2\text{O}_3 29.1-35.5 \)  
\( \text{MgO} 11.4-14.0 \)  
\( \text{SiO}_2 29.2-35.6 \)

**Loss on drying:** Less than 20 to 5% depending on grade.

**Bulk density:** Loose (0.15 g/ml)  
Tapped (0.19 g/ml)

**Specific surface area (m\(^3\)/g):** 300

**Oil adsorption capacity (ml/gm):** 2.7-3.4
**pH:** 6.0-8.0

**Safety:** It is safe with no reports of any adverse reactions.


### 4.2.4 Polyethylene glycol 400

**Synonyms:** PEG, Macrogol, Polyoxyethylene.

**CAS No:** 25322-68-3

**Formula:** H(OCH$_2$CH$_2$)$_n$OH

**Structural formula:**

![Chemical structure of PEG 400](image)

**Figure 10: Chemical structure of PEG 400**

**Physical state:** liquid.

**Solubility:** Soluble in water.

**Application:** PEG 400 used as pharmaceutical aid, dispersing agent, vehicle, and as tablet additive.

**Specification:**

**Molecular weight:** 380 – 420.

**Moisture:** 0.2% max.

**pH:** 5-7.

**Specific gravity:** From 1.12 to 1.13.

4.2.5 Citric acid

**Synonyms:** 2-hydroxypropane-1, 2, 3-tricarboxylic acid monohydrate.

**Formula for citric acid:** $C_6H_8O_7\cdot H_2O$

**Structural formula:**

![Chemical structure of citric acid](image)

**Applications:** Citric acid used as antioxidant, buffering agent and chelating agent. It is active ingredient in manufacturing of effervescent granules and tablet.

**Description:** It is white colored crystalline powder. It is odorless with intense acidic taste.

**Stability:** Loses water of crystallization.

**Incompatibilities:** Oxidizing agents, sulfides, metal nitrates, alkali carbonates, alkalis, potassium tartrate, acetates and bicarbonates.

**Safety:** Nontoxic material.

(Owen, 2006 and Nykaenen et al., 2004)

4.2.6 Aspartame

**Chemical Name:** N-α-L-Aspartyl-L-phenylalanine 1-methyl ester

**Formula:** $C_{14}H_{18}N_2O_5$
Structural Formula:

![Chemical structure of aspartame]

**Figure 12: Chemical structure of aspartame**

**Category:** Sweetening agent.

**Applications:** As sweetening agent in food, beverage products and table-top sweeteners. It is also used in pharmaceutical preparations to intensify sweet taste.

**Description:** An off white, almost odorless crystalline powder.

**Typical Properties**

**pH:** 4.5–6.0.

**Density:** 1.347 g/cm$^3$

**Solubility:** Sparingly soluble in water and slightly soluble in ethanol.

**Stability:** Stable in dry conditions.

**Storage:** In a well-closed container.

4.2.7 Crospovidone

**Synonyms:** Crospovidonum, Kollidon CL, Polyplasdone XL-10, polyvinylpolypyrrolidone.

**Formula:** (C$_6$H$_9$NO)$_n$
Structural Formula:

![Chemical structure of polystardone XL crospovidone](image)

**Figure 13: Chemical structure of polystardone XL crospovidone**

**Category:** Tablet disintegrating agent.

**Applications:** Polystardone XL crospovidone is water-insoluble. It is used as solubilizing agent. It is used in 2–5% of concentration in manufacturing of tablets as disintegrating agent. It shows good hydration capacity and results in formation of gels.

**Description:** It is free-flowing powder with white to creamy-white color. It is almost tasteless, odorless powder having hygroscopic nature.

**Typical Properties**

**Moisture content:** Absorption of moisture is approximately 60%.

**Solubility:** Insoluble in water and other organic solvents.

**Storage:** In an airtight container in a cool and dry place.

**Incompatibilities:** Compatible with other organic and inorganic pharmaceutical agent.

**Safety:** Nontoxic and nonirritant powder.

**LD50 (mouse, IP):** 12 g/kg. (Liberman et al., 1989 and Owen, 2006)

### 4.2.8 Capmul MCM

**Synonyms:** Medium chain mono-and diglycerides of caprylic acid.
**Product Type:** It is a mono-diglyceride with a class medium chain fatty acids mainly caprylic and capric. It is also a useful as emulsifying agent for the preparation of W/O type of emulsion.

**Specifications:**

**Appearance:** Liquid or semi-solid.

**Acid Value:** 2.5 max

**Moisture:** 0.5% max.

**Applications:** As a solvent, solubilizing agent, emulsifying agent, bioavailability improving agent.

**Storage:** Store in a dry place.


**4.2.9 Cremophore EL**

**Synonyms:** Polyoxy1 35 castor oil.

**Composition:** Polyoxy1 35 castor oil is a non-ionic solubilizing agent and emulsifying agent prepared by reacting ethylene oxide with castor oil. The molar ratio of castor oil to ethylene oxide is 1: 35. The main component of cremophor EL is glycerol polyethylene glycol ricinoleate. Together with fatty acid esters of poly ethylene glycol, this forms the hydrophobic (lipophilic) part of the product.

**Product type:** Cremophor EL is soluble in water but as the temperature increases Cremophor EL becomes less soluble. It is also soluble in various organic solvents.

**Specification:**

**Appearance:** Appears as pale yellow color oily liquid

**Acid value:** 2.0%

**Water:** 2.8%
pH: (10% in water) 6–8

Storage: Stored in tightly closed containers. It should be protected from light.

(Owen, 2006 and www.pharma-ingredients.basf.com)

4.2.10 Transcutol P

Synonyms: Carbitol, Transcutol, Dioxitol.

Product type: It is solvent. It is a clear, colorless liquid.

IUPAC name: 2-(2-Ethoxyethoxy)ethanol.

Empirical formula: C6H14O3.

Physical state: Colorless liquid.

Structural formula:

![Figure 14: Chemical structure of Transcutol P](image)

Features: It is solubilizing agent for poorly water soluble drugs. It improves drug penetration and permeation of drug and also acts as drug depot.

Administration Route: Oral, topical.