2.3 EXCIPIENTS REVIEW:

2.3.1 STARCH\textsuperscript{119}:

Nonproprietary Name: B.P.: Potato starch
Ph. Eur: solani amylum
USP NF: Starch

Functional category:
Glidant, tablet and capsule diluent & disintegrant, tablet binder.

Chemical name: Starch.

CAS Registry Number: 9005-25-8.

Description:
Starch occurs as an odourless and tasteless fine, white colored powder comprised of very small spherical or avoid granules.

Solubility:
Soluble in water, starch swells instantaneously in water by about 5-10 % at 37\textdegree{}C. In soluble in cold ethanol (95\%) and cold water.

Empirical Formula: \((C_{6}H_{10}O_{5})_{n}\) \(n = 300-1000\)

Applications: Binder in tablet - 5 to 25 % concentration.
Disintegrant in tablet - 3 to 15 % concentration.

Typical property:

\begin{itemize}
  \item Swelling temperature: 64 \textdegree{}C
  \item Particle size distribution: 10-100 micrometer
  \item Gelatinization at 72 \textdegree{}C.
  \item Potato starch contain 22\% of amylose
  \item Moisture content at 50\% relative humidity: 18\%.
\end{itemize}

Stability and Storage Conditions:
Dry, unheated starch is stable if protected from high humidity. When used as diluent or disintegrant in solid dosage forms, starch is considered to be inert under normal storage condition. However, heated starch solution or pastes are physically unstable and readily attacked by microorganism.
Starch should be stored in an airtight container in cool, dry place.

**Safety**: Generally regarded as non toxic and non irritant.

### 2.3.2 LACTOSE\(^{119}\):

![Chemical structure of lactose]

**Molecular weight**: 342.30 (anhydrous), 360.31 (monohydrate)

**Functional category**: Tablet and capsule diluent.

**Chemical names**:
- 4-O-β-D-galactopyranosyl-α-D-glucopyranose
- 4-(β-D-galactoside)-D-glucose.

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

**Synonyms**:
- Anhydrous Lactose NF 60M; Anhydrous Lactose NF Direct Tableting; Lactopress Anhydrous; lactosum; lattioso; milk sugar; Pharmatose DCL 21; Pharmatose DCL 22; saccharum lactis; Super-Tab Anhydrous.
Typical Properties:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angle of repose</td>
<td>39° for Pharmatose DCL 21 and 38° for Super-Tab Anhydrous.</td>
</tr>
<tr>
<td>Brittle fracture index</td>
<td>0.0362</td>
</tr>
<tr>
<td>Bonding index</td>
<td>0.0049 (at compression presume 177.8 MPa)</td>
</tr>
<tr>
<td>Density (true)</td>
<td>.589 g/cm$^3$ for anhydrous β-lactose; 1.567 g/cm$^3$ for Super-Tab Anhydrous.</td>
</tr>
<tr>
<td>Density (bulk)</td>
<td>0.68 g/cm$^3$ for Pharmatose DCL 21; 0.67 g/cm$^3$ for Pharmatose DCL 22; 0.65 g/cm$^3$ for Super-Tab Anhydrous.</td>
</tr>
<tr>
<td>Density (tapped)</td>
<td>0.88 g/cm$^3$ for Pharmatose DCL 21; 0.79 g/cm$^3$ for Pharmatose DCL 22; 0.87 g/cm$^3$ for Super-Tab Anhydrous.</td>
</tr>
<tr>
<td>Melting point</td>
<td>223.0°C for anhydrous α-lactose; 252.2°C for anhydrous β-lactose; 232.0°C (typical) for commercial anhydrous lactose.</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble in water; sparingly soluble in ethanol (95%) and ether.</td>
</tr>
</tbody>
</table>

**Description:** White to off white crystalline particles or powder, odorless and slightly sweet tasting.

**Incompatibilities:**
Lactose is incompatible with strong oxidizers. When mixtures containing a hydrophobic leukotriene antagonist and anhydrous lactose or lactose monohydrate were stored for six weeks at 40°C and 75% RH, the mixture containing anhydrous lactose showed greater moisture uptake and drug degradation.

**Safety:**
Lactose is widely used in pharmaceutical formulations as a diluent and filler-binder in oral capsule and tablet formulations. If may also be used in intravenous injections. Adverse reactions to lactose are largely due to lactose intolerance, which occurs in
individuals with a deficiency of the intestinal enzyme lactase, and is associated with oral ingestion of amounts well over those in solid dosage forms.

**Stability and Storage Conditions:**
Mold growth may occur under humid condition (80% RH and above). Lactose may develop a brown coloration on storage, the reaction being accelerated by warm, damp conditions. At 80°C and 80% RH, tablets containing anhydrous lactose have been shown to expand 1.2 times after one day. Lactose anhydrous should be stored in a well-closed container in a cool, dry place.

**Applications in Pharmaceutical Formulation or Technology:**
Anhydrous lactose is widely used in direct compression tableting applications and as a tablet and capsule filler and binder. Anhydrous lactose can be used with moisture-sensitive drugs due to its low moisture content.

### 2.3.3 MAGNESIUM STEARATE

**Synonyms:**
Magnesium octadecanoate; octadecanoic acid, magnesium salt; stearic acid, magnesium salt.

**Nonproprietary Name:**
NF: Magnesium stearate.

**Functional category:**
Tablet and capsule lubricant.

**Empirical formula:** $C_{36}H_{70}MgO_4$
**Molecular weight:** 591.3
**Structural Formula:**

\[
\text{Mg} \quad \text{CH}_3(\text{CH}_2)_{16}\text{COO} \quad \text{CH}_3(\text{CH}_2)_{16}\text{COO} \quad \text{Mg}
\]
Typical Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (bulk)</td>
<td>0.159 g/cm³</td>
</tr>
<tr>
<td>Density (tapped)</td>
<td>0.286 g/cm³</td>
</tr>
<tr>
<td>Density (true)</td>
<td>1.092 g/cm³</td>
</tr>
<tr>
<td>Flash point</td>
<td>250°C</td>
</tr>
<tr>
<td>Melting range (commercial samples)</td>
<td>117-150°C</td>
</tr>
<tr>
<td>Melting range (high purity Magnesium stearate)</td>
<td>26-130°C</td>
</tr>
<tr>
<td>Solubility</td>
<td>Practically insoluble in ethanol, ethanol (95%), ether an water; slightly soluble in warm benzene and warn ethanol (95%).</td>
</tr>
<tr>
<td>Specific surface area</td>
<td>1.6-14.8 m²/g</td>
</tr>
</tbody>
</table>

Incompatibilities

Incompatible with strong acids, alkalis, and iron salts. Avoid mixing with strong oxidizing materials. Magnesium stearate cannot be used in products containing aspirin, some vitamins, and most alkaloidal salts.

Safety

No toxicity information is available relating to normal routes of occupational exposure. Limits for heavy metals in Magnesium stearate have been evaluated in terms of Magnesium stearate worst-case daily intake and heavy metal composition.

Stability and Storage Conditions:

Stable, non-self polymerizable. Store in a cool, dry place in a well closed container.

Applications:

Tablet and capsule lubricant, glidant and antiadherent in the concentration range of 0.25 to 2.0%.
2.3.4 HYDROXY PROPYL METHYL CELLULOSE\textsuperscript{121-127}

HPMC is a partly $O$-methylated and $O$-(2-hydroxypropylated) cellulose. It is available in several grades that vary in viscosity and extent of substitution. Grades may be distinguished by appending a number indicative of the apparent viscosity.

**Nonproprietary Names:**
- *BP*: Hypromellose
- European Pharmacopoeia: Hypromellosum
- USP: Hypromellose

**Synonyms:**
Methocel; methyl hydroxypropylcellulose; Benecel®MP643, Isopto-Tears; Methopt; Poly-Tears; Tears Naturale, Methocel E, Methocel F, Methocel K Methopt, Pharmacoat ®/Metolose.

**Chemical Name:** Cellulose hydroxy methyl ether

**Empirical Formula:** $C_{56}H_{10}O_{36}$

**Molecular Weight:** Approximately 10,000–1,500,000

**Structural Formula**

Where R is H, CH$_3$, or CH$_3$CH(OH)CH$_2$
Functional Category:
Coating agent, film-former, rate controlling polymer for sustained release, stabilizing agent, suspending agent, tablet binder, viscosity increasing agent.

Applications in Pharmaceutical Formulation or Technology:

- HPMC is widely used in oral, ophthalmic and topical pharmaceutical formulations.
- In oral products, HPMC is primarily used as a tablet binder, in film coating and as a matrix for use in extended release tablet formulations.
- High viscosity grades may be used to retard the release of drugs from a matrix at levels of 10–80% w/w in tablets and capsules.
- Depending upon the viscosity grade, concentrations of 2–20% w/w are used for film-forming solutions to film coating tablets.
- Compared with methylcellulose, HPMC produces aqueous solutions of greater clarity, with fewer undispersed fibers present, and is therefore preferred in formulations for ophthalmic use.
- HPMC is also used as an emulsifier, suspending agent and stabilizing agent in topical gels and ointments.
- In addition, HPMC is used in the manufacture of capsules, as an adhesive in plastic bandages, and as a wetting agent for hard contact lenses.

Solubility:
Soluble in cold water, forming a viscous colloidal solution. Practically insoluble in chloroform, ethanol and ether. But soluble in mixtures of ethanol and dichloromethane, mixtures of methanol and dichloromethane, and mixtures of water and alcohol.

Moisture content:
HPMC absorbs moisture from atmosphere. The amount of water absorbed depends upon the initial moisture content, temperature and relative humidity of the surrounding air.
Description:
HPMC is an odorless and tasteless, white or creamy-white fibrous or granular powder.

Viscosity (2% aqueous solution):

- HPMC K100 LV : 100 cps
- HPMC K4M : 4000 cps
- HPMC K15M : 15000 cps

Typical Properties:

- pH
  
  pH = 5.5–8.0

- Melting point
  
  Chars at 225°C–230°C

- Specific gravity
  
  1.26

- Bulk density
  
  0.341g/m³

- Ash value
  
  1.5–3.0%

A wide range of viscosity types are commercially available.

Stability and Storage Conditions:

➢ HPMC powder is a stable material, although it is hygroscopic after drying.

➢ Solutions are stable at pH 3–11. Increasing temperature reduces the viscosity of solutions.

➢ HPMC undergoes a reversible sol–gel transformation upon heating and cooling, respectively.

➢ HPMC powder should be stored in a well-closed container, in a cool, dry place.
Typical Viscosity Values for 2% (w/v) Aqueous Solutions of Methocel Viscosities
Measured at 20°C

<table>
<thead>
<tr>
<th>Methocel product</th>
<th>USP 28 designation</th>
<th>Nominal viscosity (mPa s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methocel K100 Premium LVEP</td>
<td>2208</td>
<td>100</td>
</tr>
<tr>
<td>Methocel K4M Premium</td>
<td>2208</td>
<td>4000</td>
</tr>
<tr>
<td>Methocel K15M Premium</td>
<td>2208</td>
<td>15000</td>
</tr>
<tr>
<td>Methocel K100M Premium</td>
<td>2208</td>
<td>100000</td>
</tr>
<tr>
<td>Methocel E4M Premium</td>
<td>2910</td>
<td>4000</td>
</tr>
<tr>
<td>Methocel F50 Premium</td>
<td>2906</td>
<td>50</td>
</tr>
<tr>
<td>Methocel E10M Premium CR</td>
<td>2906</td>
<td>10000</td>
</tr>
<tr>
<td>Methocel E3 Premium LV</td>
<td>2906</td>
<td>3</td>
</tr>
<tr>
<td>Methocel E5 Premium LV</td>
<td>2906</td>
<td>5</td>
</tr>
<tr>
<td>Methocel E6 Premium LV</td>
<td>2906</td>
<td>6</td>
</tr>
<tr>
<td>Methocel E15 Premium LV</td>
<td>2906</td>
<td>15</td>
</tr>
<tr>
<td>Methocel E50 Premium LV</td>
<td>2906</td>
<td>50</td>
</tr>
<tr>
<td>Metolose 60SH</td>
<td>2910</td>
<td>50, 4000, 10 000</td>
</tr>
<tr>
<td>Metolose 65SH</td>
<td>2906</td>
<td>50, 400, 1500, 4000</td>
</tr>
<tr>
<td>Metolose 90SH</td>
<td>2208</td>
<td>100, 400, 4000, 15000</td>
</tr>
</tbody>
</table>

Safety:
Hypromellose is widely used as an excipient in oral and topical pharmaceutical formulations. It is also used extensively in cosmetics and food products. Hypromellose is generally regarded as a nontoxic and nonirritant material, although excessive oral consumption may have a laxative effect. The WHO has not specified an
acceptable daily intake for hypromellose since the levels consumed were not considered to represent a hazard to health.

LD$_{50}$ (mouse, IP): 5 g/kg

LD$_{50}$ (rat, IP): 5.2 g/kg

**Handling precautions:**

Observe normal precautions appropriate to the circumstances and quantity of material handled. Hypromellose dust may be irritant to the eyes and eye protection is recommended. Excessive dust generation should be avoided to minimize the risks of explosion. Hypromellose is combustible.

**Regulatory status:** Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (ophthalmic preparations, oral capsules, suspensions, syrups and tablets, topical and vaginal preparations). Included in nonparenteral medicines licensed in the UK.

**2.3.5 CARBOPOL$^{128-132}$**

It is a synthetic high molecular weight polymer of acrylic acid crosslinked with either allyl sucrose or allyl ethers of of pentaerythritol they contain between 56-68% of carboxylic acid groups calculated on the dry bases the carboxylic group provided by the acrylic acid back bone of the polymer are responsible for many of the product characteristic

**Nonproprietary Name**

- BP: Carbomers
- PhEur: Carbomera
- USPNF: Carbomer

**Synonyms:**

Acrilamet; acrylic acid polymer; Carbopol; carboxy polymethylene, polyacrylic acid; carboxyvinyl polymer; Pemulen; Ultrez.
Chemical Name: Carboxy polymethylene

Empirical Formula: \((C_3H_4O_2)^n (-C_3H_5\text{ sucrose})\)

Molecular Weight: \(1\times10^6\) and \(4\times10^5\)

Structural Formula

Grades


Functional Category:
Bioadhesive; emulsifying agent; release-modifying agent; suspending agent; tablet binder; viscosity-increasing agent.

Applications in Pharmaceutical Formulation or Technology:
Carbomers are mainly used in liquid or semisolid pharmaceutical formulations as suspending or viscosity-increasing agents.
Carbomer having low residuals only of ethyl acetate, such as carbomer 971P or 974P, may be used in oral preparations, in suspensions, tablets, or sustained release tablet formulations.
In tablet formulations, carbomers are used as dry or wet binders and as a rate controlling excipient. Carbomer resins have also been investigated in the preparation of sustained-release matrix beads, as enzyme inhibitors of intestinal proteases in peptide-containing dosage forms.
Carbomers are also employed as emulsifying agents in the preparation of oil-in-water emulsions for external use.
Description:

Carbomers are white-colored, ‘fluffy’, acidic, hygroscopic powders with a slight characteristic odor.

Typical Properties

- **pH**: 2.7–3.5
- **Specific gravity**: 1.41
- **Melting point**: 260°C
- **Bulk density**: 1.76–2.08 g/cm³
- **Tapped density**: 1.4 g/cm³

Moisture content:

Normal water content is up to 2% w/w. However, carbomers are hygroscopic and a typical equilibrium moisture content at 25°C and 50% relative humidity is 8–10% w/w. The moisture content of a carbomer does not affect its thickening efficiency, but an increase in the moisture content makes the carbomer more difficult to handle because it is less readily dispersed.

Particle size distribution:

Primary particles average about 0.2 μm in diameter. The flocculated powder particles average 2–7 μm in diameter and cannot be broken down into the primary particles. Recently, a granular carbomer having a particle size in the range 180–425 μm has been introduced. Its bulk and tap densities are also higher than those of other carbomers.

Solubility:

Soluble in water and, after neutralization, in ethanol (95%) and glycerin.

Stability and Storage Conditions:

Carbomers are stable, hygroscopic materials that may be heated at temperatures below 104°C for up to 2 h without affecting their thickening efficiency. However, exposure to excessive temperatures can result in discoloration and reduced stability. Complete decomposition occurs with heating for 30 minutes at 260°C. Dry powder forms of
carbomer do not support the growth of molds and fungi. Carbomer powder should be stored in an airtight, corrosion-resistant container in a cool, dry place. The use of glass, plastic, or resin-lined containers is recommended for the storage of formulations containing carbomer.

**Typical Properties:**

**Pharmacopeial specifications for carbomers.**

<table>
<thead>
<tr>
<th>Test</th>
<th>PhEur 2005</th>
<th>USPNF 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Characters</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>Aqueous viscosity (mPa s)</td>
<td>300–115 000</td>
<td>—</td>
</tr>
<tr>
<td>Carbomer 934 (0.5% w/v)</td>
<td>—</td>
<td>30 500–39 400</td>
</tr>
<tr>
<td>Carbomer 934P (0.5% w/v)</td>
<td>—</td>
<td>29 400–39 400</td>
</tr>
<tr>
<td>Carbomer 940 (0.5 w/v)</td>
<td>—</td>
<td>40 000–60 000</td>
</tr>
<tr>
<td>Carbomer 941 (0.5 w/v)</td>
<td>—</td>
<td>4 000–11 000</td>
</tr>
<tr>
<td>Carbomer 1342 (1.0% w/v)</td>
<td>—</td>
<td>9 500–26 500</td>
</tr>
</tbody>
</table>

**2.3.6 CROSPOVIDONE**

**Synonyms:**
Cross linked povidone; Kollidon CL; Polyplasdone XL.

**Chemical Name and CAS Registry Number:**
1-Ethenyl-2-pyrrolidinone homopolymer [9003-39-8]

**Empirical Formula and Molecular Weight:**
(C₆H₉NO)ₙ >1 000 000
**Functional Category:**
Tablet disintegrant.

**Applications in Pharmaceutical Formulation or Technology:**
Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct-compression or wet- and dry-granulation methods.
It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels.
Crospovidone strongly influences disintegration of analgesic tablets. Larger particles provide a faster disintegration than smaller particles.
Crospovidone can also be used as a solubility enhancer. With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs. The drug is adsorbed on to crospovidone in the presence of a suitable solvent and the solvent is then evaporated. This technique results in faster dissolution rate.

**Description:**
Crospovidone is a white to creamy-white, finely divided, free-flowing, practically tasteless, odorless or nearly odorless, hygroscopic powder.

**Typical Properties:**
**Acidity/alkalinity:** pH = 5.0–8.0 (1% w/v aqueous slurry)

**Density:** 1.22 g/cm³

**Solubility:** Practically insoluble in water and most common organic solvents.

**Stability and Storage Conditions:**
Since crospovidone is hygroscopic, it should be stored in an airtight container in a cool, dry place.
Incompatibilities:
Crospovidone is compatible with most organic and inorganic pharmaceutical ingredients. When exposed to a high water level, crospovidone may form molecular adducts with some materials

2.3.7 MICROCRYSTALLINE CELLULOSE¹³⁵,¹³⁶

Synonyms:
Avicel, Celex, cellulose gel, Celphere, Emocel, Pharmacel, Tabulose.

Nonproprietary Name:
BP: Microcrystalline Cellulose
Ph.Eur. Cellulosum Microcristsllium
USP NF: Microcrystalline Cellulose

Chemical Name: Cellulose
Empirical Formula: \((C_6H_{10}O_5)\)
Molecular Weight: ~ 36000
Functional Category: Tablet Disintegrant (5-15%), Adsorbent, Tablet and capsule diluent.

Typical Properties:
pH: 5.0 to 7.5
Melting point: Chars at 260-270ºc
Angle of repose: 34.4º for Emcocel 90m
Density (bulk): 0.32 g/cm² for Avicel pH 101; 0.29 g/cm² for Emcocel 90m
Flowability: 1.41 g/s for Emcocel 90m
Sulfated ash: ≤ 0.1%

Description:
Microcrystalline cellulose is purified, partially depolymerized cellulose that occurs as a white, odorless, tasteless, crystalline powder composed of porous particles. It is commercially available in different particle sizes and moisture grades that different properties and applications.
Pharmaceutical Uses:
Microcrystalline cellulose is widely used in pharmaceuticals, primarily as a binder / diluent in oral tablet and capsule formulation where it is used in both wet granulation and direct compression processes. In addition to its use as binder / diluent, microcrystalline cellulose also has some lubricant and disintegrant properties that make it useful in tableting.

Solubility:
Slightly soluble in 5% w/v sodium hydroxide solution but practically insoluble in water, dilute acids and most organic solvents.

Moisture content: Typically less than 5% w/w. However different grades may contain varying amounts of microcrystalline cellulose in hygroscopic

Incompabilities: Incompatible with strong oxidizing agents

Stability and storage:
Under humid condition (80% & above) mold growth may occur. Lactose may develop a brown coloration on storage; the reaction is accelerated by warm & damp condition. It should be sorted in a well closed container in a cool, dry place.

Safety:
It is regarded as a nontoxic & non irritant material. Adverse reaction may be seen in a person with deficiency of intestinal enzyme lactase.

2.3.8 Sodium Bicarbonate137,138:
Synonyms: Backing soda, E500, Monosodium carbonate, Sodium acid carbonate, Sodium hydrogen carbonate.
Nonproprietary Name:
B.P.: Sodium Bicarbonate.
USP: Sodium Bicarbonate
Chemical name: Carbonic acid monosodium salt.

Molecular weight: 84.01

Structural formula: NaHCO₃

Description:
Sodium Bicarbonate occurs as odourless, White crystalline powder with saline, slightly alkaline taste. Crystal structure is monolithic prisms. Commercially different particle size from fine powder to free flowing granules available.

Solubility:
Practically insoluble in Ethanol (95%) and Ether at 20°C. In water 1 in 11 at 20°C and 1 in 4 at 100°C.

Functional Category: Alkalizing agent, Therapeutic agent.

Typical Properties:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidity/alkalinity</td>
<td>pH=8. for a freshly prepared 0.1 M aqueous solution at 25°C; alkalinity increases on standing, agitation, or heating</td>
</tr>
<tr>
<td>Density (bulk)</td>
<td>0.869 g/cm³</td>
</tr>
<tr>
<td>Density (tapped)</td>
<td>1.369 g/cm³</td>
</tr>
<tr>
<td>Density (true)</td>
<td>2.173 g/cm³</td>
</tr>
<tr>
<td>Freezing point depression</td>
<td>0.381°C (1% w/v solution)</td>
</tr>
<tr>
<td>Melting point</td>
<td>270°C (with decomposition)</td>
</tr>
<tr>
<td>Moisture content</td>
<td>Below 80% relative humidity, the moisture content is less than 1% w/w. Above 85% relative humidity, sodium bicarbonate rapidly absorbs excessive amounts of water and may start to decompose with loss of carbon dioxide.</td>
</tr>
</tbody>
</table>
Incompatibilities:
Sodium bicarbonate reacts with acids, acidic salts, and many alkaloidal salts, with the evolution of carbon dioxide. Sodium bicarbonate can also intensity the darkening of salicylates. In powder mixtures, atmospheric moisture or water of crystallization from another ingredient is sufficient for sodium bicarbonate to react with compounds such as boric acid or alum. In liquid mixtures containing bismuth subnitrate, sodium bicarbonate reacts with the acid formed by hydrolysis of the bismuth salt. In solution, sodium bicarbonate has been reported to be incompatible with many drug substances such as ciprofloxacin, amiodarone, nicardipine, and levofloxacin.

Safety:
When used as an excipient, sodium bicarbonate is generally regarded as an essentially nontoxic and nonirritant material.

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 250-300°C, or a short time, sodium bicarbonate is completely converted into anhydrous sodium carbonate. However, the process is both time- and temperature-dependent, with conversion 90% complete within 75 minutes at 93°C. The reaction proceeds via surface-controlled kinetics; when sodium bicarbonate crystals are heated for a short period of time, very fine needle-shaped crystals of anhydrous sodium carbonate are formed on the sodium bicarbonate surface.

Applications in Pharmaceutical Formulation or Technology:
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; 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. When the tablets or granules come into contact with water, a chemical reaction occurs, carbon dioxide is evolved, and the product disintegrates.
2.3.9 GUAR GUM\textsuperscript{138-39}. 

The gum consists of the pulverized endosperm of the seed of \textit{Cyamopsix tetragonolobus} belonging to family Leguminosae. The seed hull can be removed by grinding, after soaking in sulfuric acid or water or by charring. The embryo (germ) is removed by differential grinding. The separated endosperm is ground to different particle sizes depending upon final application.

\textbf{Description:}

Odorless, bland in taste; white to yellowish-white powder.

\textbf{Molecular weight:} 2, 20,000

\textbf{Chemical Name:} Galactomannan polysaccharide.

\textbf{Non-proprietary name:} N F: Gaur gum.

\textbf{Viscosity (1\% aqueous solution):} 2,000 – 22,500 cps.

\textbf{Solubility:}

Gaur gum forms viscous colloidal dispersions when hydrated in cold water.

\textbf{Stability:}

Stable in solution over a pH range of 1-10.5. Prolong heating degrades the viscosity.

Gaur gum is recognised by the FDA.

\textbf{Applications:}

Guar gum is used as tablet binder in concentration 1-10. It is used as suspending and viscosity-increasing agent in various dosage forms. It is again used as emulsion stabiliser.
2.3.10 SODIUM ALGINATE\textsuperscript{138-39}

Non proprietary names (BP, USP, NF) : Sodium Alginate

Description: 
Sodium alginate occurs as an odorless and tasteless, while to pale yellowish brown colored powder.

Solubility: 
Practically insoluble in ethanol, ether, chloroform and ethanol/water mixtures in which ethanol content is greater than 30\%. Also, practically insoluble in other organic solvents and aqueous acidic solutions in which the pH is less than 3. Slowly soluble in water, forming a viscous colloidal solution.

Viscosity: 
Various grades sodium alginate are commercially available that yield aqueous solutions of varying viscosity (20-400 cP at 20\°C). Viscosity may vary depending on temperature, concentration, pH, or the presence of metal ions. Above pH 10, viscosity decreases.

Application: 
Stabilizing agent; suspending agent; tablet and capsule disintegrate; tablet binder; viscosity increasing agent. Used as a diluent in capsule formulations. It is also used for micro encapsulation of drugs, preparation of nanoparticles.

Incompatibilities It is incompatible with acridine derivatives, crystal violet, PMA and PMN, calcium salts, heavy metals and ethanol in concentration greater than 5\%.

Stability: 
It is hygroscopic material, although it is stable if stored low humidities and cool temperature.
2.3.11 XANTHAN GUM\textsuperscript{138-39}

**Non proprietary names**

BP, USP, NF : Xanthan gum

**Synonyms:** Corn sugar gum; Keltrol

**Solubility:**

Practically insoluble in ethanol and ether; soluble in cold or warm water.

**Viscosity:**

1200–1600 mPa s (1200–1600 cP) for a 1\% w/v aqueous solution at 25°C.

**Application:**

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. It is nontoxic, compatible with most other pharmaceutical ingredients, and has good stability and viscosity properties over a wide pH and temperature range; Xanthan gum gels show pseudoplastic behavior, the shear thinning being directly proportional to the shear rate. The viscosity returns to normal immediately on release of shear stress.

**Incompatibilities:**

Xanthan gum is an anionic material and is not usually compatible with cationic surfactants, polymers, or preservatives as precipitation occurs. Anionic and amphoteric surfactants at concentrations above 15\% w/v cause precipitation of xanthan gum from a solution.

Under highly alkaline conditions, polyvalent metal ions such as calcium cause gelation or precipitation; this may be inhibited by the addition of a glucoheptonate sequestrant. The presence of low levels of borates (<300 ppm) can also cause gelation. This may be avoided by increasing the boron ion concentration or by lowering the pH of a formulation to less than pH 5. The addition of ethylene glycol, sorbitol, or mannitol may also prevent this gelation.
Stability:
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. Xanthan gum solutions of less than 1% w/v concentration may be adversely affected by higher than ambient temperatures: for example, viscosity is reduced. Solutions are also stable in the presence of enzymes, salts, acids, and bases. Safety: Xanthan gum is widely used in oral & topical pharmaceutical formulation, cosmetics and food products and is generally regarded as nontoxic & nonirritant at the level employed as pharmaceutical excipients.
2.3.12 Povidone[^138-39]

**Synonyms:** E1201; Kollidon; Plasdon, poly [1-(2-oxo-1-pyrrolidinyl) ethylene]; polyvidone; polyvinylpyrrolidone; PVP; 1-vinyl-2-pyrrolidinone polymer.

**Typical Properties:**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidity/alkalinity</td>
<td>pH = 3.0-7.0 (5% w/v aqueous solution).</td>
</tr>
<tr>
<td>Density (bulk)</td>
<td>0.29-0.39 g/cm³ for Plasdone.</td>
</tr>
<tr>
<td>Density (tapped)</td>
<td>0.39-0.54 g/cm³ for Plasdone.</td>
</tr>
<tr>
<td>Density (true)</td>
<td>1.180 g/cm³</td>
</tr>
<tr>
<td>Flow ability</td>
<td></td>
</tr>
<tr>
<td>20 g/s for povidone K-15;</td>
<td></td>
</tr>
<tr>
<td>16 g/s for providone K-29/32</td>
<td></td>
</tr>
<tr>
<td>Melting point</td>
<td>Softens at 150°C</td>
</tr>
<tr>
<td>Moisture content</td>
<td>Povidone is very hygroscopic, significant amounts of moisture being absorbed at low relative humidities.</td>
</tr>
<tr>
<td>Particle size distribution</td>
<td>o Kolslidon25/30: 90%&gt;50μm, 50%&gt;100 μm, 5%&gt;200μm;</td>
</tr>
<tr>
<td></td>
<td>o Killidon 90:90%&gt;200 μm, 95%&gt;250 μm.</td>
</tr>
<tr>
<td>Solubility</td>
<td>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.</td>
</tr>
<tr>
<td>Viscosity (dynamic)</td>
<td>The viscosity of aqueous povidone solutions depends on both the concentration and the molecular weight of the polymer employed.</td>
</tr>
</tbody>
</table>
Incompatibilities:
Povidone is compatible in solution with a wide range of inorganic salts, natural and synthetic resins, and other chemicals. It forms molecular adducts in solution with sulfathiazole, sodium salicylate, salicylic acid, phenobarbital, tannin, and other compound. The efficacy of some preservative, e.g. thimerosal, may be adversely affected by the formation of complexes with povidone.

Safety:
Povidone is widely used as an excipient, particularly in oral tablets and solution. When consumed orally, povidone may be regarded as essentially nontoxic since it is not absorbed from the gastrointestinal tract or mucous membrane. Povidone additionally has no irritant effect on the skin and causes no sensitization.

Stability and Storage Conditions:
Povidone darkens to some extent on heating at 150°C, with a reduction in aqueous solubility. It is stable to a short cycle of heat exposure around 110-113°C; steam sterilization of an aqueous solution does not alter its properties. Aqueous solutions are susceptible to mold growth and consequently require the addition of suitable preservatives. Povidone may be stored under ordinary conditions without undergoing decomposition or degradation. However, since the powder is hygroscopic, it should be stored in an airtight container in a cool, dry place.

Applications in Pharmaceutical Formulation on Technology:
Although povidone is used in a variety of pharmaceutical formulations, it is primarily used in solid-dosage forms. In tableting, povidone solutions are use 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.

### 2.3.13 Citric Acid\(^{140}\)

**Synonyms:** E330; 2-hydroxypropane-1, 2, 3-tricarboxylic acid monohydrate.

**Typical Properties:**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density</td>
<td>1.542 g/cm(^3)</td>
</tr>
<tr>
<td>Heat of combustion</td>
<td>-1972 kJ/mol (-471.4 kcal/mol)</td>
</tr>
<tr>
<td>Heat of solution</td>
<td>-16.3 kJ/mol (-3.9 kcal/mol) at 25°C</td>
</tr>
<tr>
<td>Hygroscopicity</td>
<td>At relative humidities less than about 65% citric acid monohydrate effloresces at 25°C, the anhydrous acid being formed at relative humidities less than about 40%. At relative humidities between about 65% and 75%, citric acid monohydrate absorbs insignificant amounts of moisture, but under more humid conditions substantial amount of water are absorbed.</td>
</tr>
<tr>
<td>Melting point</td>
<td>≥100°C (softens at 75°C)</td>
</tr>
<tr>
<td>Particle size distribution</td>
<td>Various grades of citric acid monohydrate with different particle sizes are commercially available.</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble 1 in 1.5 parts of ethanol (95%) and 1 in less than 1 part of water; sparingly soluble in ether.</td>
</tr>
<tr>
<td>Viscosity (dynamic)</td>
<td>6.5 mPa s (6.5 cP) for a 50% w/v aqueous solution at 25°C.</td>
</tr>
</tbody>
</table>
Dissociation constant:
1. $\text{pK}_{\text{a1}}$: 3.128 at 25°C;
2. $\text{pK}_{\text{a2}}$: 4.761 at 25°C;
3. $\text{pK}_{\text{a3}}$: 6.396 at 25°C.

**Incompatibilities:**
Citric acid is incompatible with potassium tartrate, alkali and alkaline earth carbonates, acetates, and sulfides. Incompatibilities also include oxidizing, bases, reducing agents, and nitrates. It is potentially explosive in combination with metal nitrates. On storage, sucrose may crystallize from syrups in the presence of citric acid.

**Safety:**
Orally ingested citric acid is absorbed and is generally regarded as a nontoxic material when used as an excipient. However, excessive or frequent consumption of citric acid has been associated with erosion of the teeth.

**Stability and Storage Conditions:**
Citric acid monohydrate losses water of crystallization in dry air or when heated to about 40°C. It is slightly deliquescent in moist air. Dilute aqueous solutions of citric acid may ferment on standing. The bulk monohydrate or anhydrous material should be stored in airtight containers in a cool, dry place.

**Applications in Pharmaceutical Formulation or Technology:**
Citric acid (as either the monohydrate or anhydrous material) is widely used in pharmaceutical formulations and food products, primarily to adjust the pH of solutions. It has also been used experimentally to adjust the pH of tablet matrices in enteric-coated formulations for colon-specific drug delivery. Citric acid monohydrate is used in the preparation of effervescent granules, while anhydrous citric acid is widely used in the preparation of effervescent granules, tablets. Citric acid has also been shown to improve the stability of spray-dried insulin powder in inhalation formulations. In food products,
Citric acid is used as a flavor enhancer for its tart, acidic taste. Citric acid monohydrate is used as a sequestering agent and antioxidant synergist. It is also a component of anticoagulant citrate.

2.3.14 Talc\(^{140}\)

**Synonyms:**
Altalc; E553b; hydrous magnesium calcium silicate; hydrous magnesium silicate; Lezunac Pharma; magnesium hydrogen metasilicate; Magsil Osmanthus; Magsil Star; powdered talc; purified French chalk; Purtalc; soapstone; steatite; Superiore.

**Typical Properties:**

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidity/alkalinity</td>
<td>pH=7-10 for a 20% w/v aqueous dispersion.</td>
</tr>
<tr>
<td>Hardness (Mohs)</td>
<td>1.0-1.5</td>
</tr>
<tr>
<td>Moisture content</td>
<td>Talc absorbs insignificant amounts of water at 25°C and relative humidities up to about 90%.</td>
</tr>
<tr>
<td>Particle size distribution</td>
<td>Varies with the source and grade material. Two typical grades are ≥ 99% through a 74 μm (#200 mesh) or ≥99% through a 44 μm (#325 mesh).</td>
</tr>
<tr>
<td>Refractive Index</td>
<td>1.54 – 1.59</td>
</tr>
<tr>
<td>Solubility</td>
<td>Practically insoluble in dilute acids and alkalis, organic solvents, and water</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>2.7-2.8</td>
</tr>
</tbody>
</table>

**Incompatibilities:**

Incompatible with quaternary ammonium compounds.

**Safety:** Although talc has been extensively investigated for its carcinogenic potential and it has been suggested that there is an increased risk of ovarian cancer in women using talc, the evidence is inconclusive. However, talc contaminated with asbestos has been
proved to be carcinogenic in humans, and asbestos-free grades should therefore be used in pharmaceutical products.

**Stability and Storage Conditions:**
Talc is a stable material and may be sterilized by heating at 160°C for not less than 1 hour. It may also be sterilized by exposure to ethylene oxide or gamma irradiation. Talc should be stored in a well-closed container in a cool, dry place.

**Applications in Pharmaceutical Formulation or Technology:**
Talc was once widely used in oral solid dosage formulations as a lubricant and diluents, although today it is less commonly used. However, it is widely used as a dissolution retardant in the development of controlled-release products.
Talc is also used 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 therefore frequently contain microorganisms and should be sterilized when used as a dusting powder.
Talc is additionally used to clarify liquids and is also used in cosmetics and food products, mainly for its lubricant properties.

### 2.3.15 Isapgulla husk (Psyllium)

**Synonyms**: ispaghula, isabgol, psyllium

**Biological Name**: Plantago ovata (family - Plantaginaceae)

**Properties**:
- **pH**: 4-5
- The kinematic viscosity of (0.5%, w/v) Aqueous dispersion: - 4-6 centistokes.
- **Swelling factor**: 10-14

**Description**:
Psyllium mucilage is obtained from the seed coat of Plantago ovata by milling the outer layer of the seeds. It has been evaluated for its tablet binding properties, but also to form
hydrogels through radiation-induced cross-linking for controlled release of 5-fluorouracil as model drug. Psyllium husk was used in combination with other excipients such as hydroxypropyl methylcellulose to prepare novel sustained release, swellable and bioadhesive gastroretentive drug delivery systems for Aceclofenac. The incorporation of HPMC K4M into psyllium husk granule was observed to reduce the immediate swelling of the matrix and thus reduce its release. It is white fibrous material, hydrophilic in nature and forms a clear colorless mucilaginous gel by absorbing water

Pharmaceutical Uses:
The seed and husk of the isabgol are widely used in pharmaceutical industry as demulcent, emollient, laxative, as an adjunct to dietary and drug therapy on lipid and glucose levels, in patients with type II diabetes, and in the treatment of dysentery. The seed and husk of the isabgol contains mucilage which is present in the epidermis of the seed. It is official in IP, BP, and USP. It is used in food and pharmaceuticals at a dose level of 5-6 g twice a day.
Psyllium seed husk is used as binder, disintegrant and release retardant. Psyllium seed husk is used as binder, disintegrant and release retardant.

Solubility:
They are soluble in water, expanding and becoming mucilaginous when wet.

Safety: it is regarded as a nontoxic & non irritant material.

2.3.16 Accurel microporous polymer (MP1000)\textsuperscript{143-44}

Accurel MP is the name given to a group of microporous polymer products made from commercially available resins. Some common resins available in microporous form are PP, LLDPE, LDPE, HDPE and PA.

Microporous structures act like tiny sponges with the ability to absorb several times their own weight. When liquids or meltable solids are mixed with the porous polymer, the micron-size voids in the polymer are filled by capillary absorption. As the mixing is done
at room temperature, Accurel MP is especially suitable for thermally sensitive additives. When fully loaded with the liquid additive, the system remains dry and free-flowing. In these applications, the large inner surface of the Accurel MP resin, with its accompanying adhesion forces, is utilized in combination with the cell and pore structure of the matrix to retain liquid within the polymer carrier.

Supplier- Membrana GmbH, Obernburg, Germany

**Hazards identification:** Not classified as hazardous and dangerous preparation.

**Handling and storage:** Follow normal industrial hygiene standards.

**Storage:** Store at ambient temperatures. Store in a dry place.

**Physical and chemical properties :**

- Appearance: powder/ pellets/ cylinders/ tubes
- Colour: White/ Cream
- Odour: Odourless
- Melting point/ range: > 70°C
- Bulk density: 100-300 kg/m³
- Solubility: Practically insoluble in water

**Toxicity :**

Oral LD50- > 2000 mg/kg, Dermal LD50-expected to be > 2000 mg/kg