2.1 Ondansetron Hydrochloride

Fig No 15: Molecular Structure of Ondansetron Hydrochloride

2.1.1 General Information

**IUPAC Name:** (±) 1, 2, 3, 9- tetrahydro-9- methyl-3-[(2- methyl-1H-imidazol-1-yl) methyl]- 4H-carbazol-4-one

**Molecular Formula:** C\textsubscript{18}H\textsubscript{19}N\textsubscript{3}O•HCl•2H\textsubscript{2}O

**Molecular Weight:** 365.9

**Melting Range:** 178.5\(^{0}\)-179.5\(^{0}\) C

**Bioavailability:** Approximately 60%

**pKa:** 7.4

**Plasma protein binding:** Approximately 70-75%

**Plasma half life:** 3-4 hours.

**Stability:** Stable molecule
**Solubility:** Soluble in aqueous-solutions, solubility decline with increase pH above 5.7. It is sparingly soluble in water & alcohol, slightly soluble in dichloromethane and isopropyl-alcohol, solubilises in methyl alcohol.

**Colour & taste:** White or off white powder and taste is bitter.

**Category:** Serotonin receptor (5HT₃) antagonist (antiemetics)

### 2.1.3 Clinical Pharmacology:

#### Pharmacokinetics

Absorption of Ondansetron is good throughout gastro-intestinal tract and it undergo little first pass biotransformation. Upon ingestion of a 8mg tablet, mean bioavailability in healthy subjects, is about 56 %. AUCs from a 16mg tablets were 24 % larger than forecasted from an 8mg tablet, indicating decrease in first pass metabolism at high peoral dose. Presence of food enhances bioavailability of drug but unaffected by antacids. It comprehensively get metabolize in human, with around 5% of a radio-labelled doses recuperated as the parent substance from urinary route. Primarily it undergoes metabolism by hydroxylations at indole-ring following sulphate/glucuronide-conjugation. However some non-conjugated metabolite show pharmacologic-activity, they are not present in systemic circulation at concentration possible to considerably add to the biological-activity the drug. A lesser $V_d$ (volume of distribution) in women, slower clearance, and high absolute-bioavailability results in elevated plasma concentration of drug.

### 2.1.4 Therapeutic Uses

- To prevent nausea/vomiting related with preliminary and repeated course of emetogenic cancer-chemotherapy, also in high doses cisplatin.

- To prevent post operative vomiting, nausea. For Ondansetron unlike other-antiemetics, regular prophyalaxis is not suggested for patient which have slight expectations that nausea/vomiting will arise post-operatively.

### 2.1.5 Dose and Dosage Regimen
To prevent nausea/vomiting induced by extremely emetogenic cancer-chemotherapy, the suggested peroral dose for adults is 24mg to be taken as three 8mg doses ingested 30min. prior to beginning of single day emetogenic-chemotherapy, including cisplatin \( \geq 50\text{mg/m}^2 \).

2.1.6 Contraindication

The simultaneous administration of apomorphin with Ondensetron should be restricted. It may cause deep hypo-tension and unconsciousness.

2.1.7 Adverse reactions

CNS: Patients taking ondansetron may rarely suffer extra-pyramidal reaction.

Hepatic: It is reported of hepatic disfunction and fatality in patient suffering cancer taking simultaneous medication of significantly hepatotoxic cyto-toxic chemotherapy and antibiotic.

Other: Unusual cases of spasm in bronchi, anaphylaxis, tachycardia, electrocardiographic alteration, vascular-occlusive event and hypokalemia, also grandmal seizure has reported.

2.2 Ketoprofen

![Molecular Structure of Ketoprofen](image)

**Fig No 16:** Molecular Structure of Ketoprofen

2.2.1 General Information

**Chemical name:** Ketoprofen is 2-(3-benzoylphenyl) propanoic acid
**Molecular formula:** \( C_{16}H_{14}O_3 \)

**Molecular weight:** 254.2806

**Melting point:** 92\(^\circ\)C-97\(^\circ\)C

**Functional Categories:** Anti-inflammatory; analgesic.

**Solubility of drug:** Freely soluble in chloroform, ether, ethyl alcohol (95 %) and in acetone. It is practically not soluble in water.

**Standards:** Ketoprofen contains less than 101.0 percent and more than 98.5 percent of \( C_{16}H_{14}O_3 \), calculated on the dried basis.

**Storage:** Protected from light. Store in well-closed containers.

**Half Life:** 1.1-4 hours

**Biotransformation:** Hepatic

**Dose:** 75mg TDS

### 2.2.2 Mechanism of action:

Anti-inflammatory effect of ketoprofen is supposed to be because of COX-2-inhibition, which is concerned for prostaglandin-synthesis by means of the arachidonic-acid pathways. It decreases level of prostaglandin which is responsible to cause pain, inflammation and fever. Ketoprofen inhibits nonspecifically the cyclooxygenase and COX-1-inhibition may originate few side-effects, like ulceration and GIT-upset. It is considered to have antibradykinin action, also lysosomal-membrane stabilizing actions. Due to its action on the hypothalamus it shows antipyretic effects, results in vasodilation, an enhanced peripheral blood flow followed by heat-dissipation. [D. Perumal., 2001]

### 2.2.3 Pharmacokinetic and metabolism:

Ketoprofen shows rapid absorption upon peroral ingestion, its peak-plasma levels are observed after 15-30 mins. The plasma half life is about 1.1-4 hrs. Ketoprofen
comprehensively (99 %) binds to plasma-protein; however the drug occupies merely a portion of the total drug binding sites at usual-concentration. Ketoprofen goes slow in the synovial-space and can retain there at greater concentration as the concentration in plasma decreases. The Ketoprofen get excreted rapidly and completely. In excess of 90% of an administered dose excretes in urine as metabolite or their conjugate. The chief metabolites may be hydroxylates and carboxylates complexes. [Chong-Kook Kim, 1994]

2.2.4 Side effect:

Overdose Ketoprofen may cause abdominal pain, vomiting and drowsiness. These side-effects are generally serene and largely involving the GIT. Dyspepsia is the main frequent adverse effect in GIT (11 % patient). It may cause diarrhea, nausea, constipation and abdominal-pain in more than 3 % of patient.

2.2.5 Drug Interaction:

Ketoprofen can leads to elevation of cyclosporine serum-levels and might boost the nephro-toxicity of cyclosporine. Ketoprofen may decrease the renal-excretion of methotrexate, thus increases threat of methotrexate-toxicity. The ketoprofen can increase the anticoagulant effect of anisindione. The NSAID, ketoprofen, can enhance the anti-coagulant property of acenocoumarol. The NSAID, ketoprofen, can enhance the anti-coagulant property of dicumarol. The anti-platelet effect of ketoprofen might raise the hemorrhage threat related with warfarin. Alternative treatment should be considered for the indications of bleed in simultaneous therapy. Simultaneous use of Ketoprofen and Telmisartan increases the chances of acute-renal-failure and hyper-kalemia. Renal-function at the commencement and throughout therapy should be monitored. [Yasunori Sato, 1996]
2.3 Glipizide:

Chemically glipizide is 1- cyclohexyl-3- [[p-(2- (5-methyl) pyrazine carboxamido) ethyl] phenyl] sulfonylurea.

![Molecular Structure of Glipizide](image)

**Fig No. 17:** Molecular Structure of Glipizide

### 2.3.1 General Information:

- **Mol. Formula:** C21H27N5O4S
- **Mol.Wt.** 445.55
- **Synonym:** Glydiazinamide

**Nomenclature:** 1-cyclohexyl-3- [4- [2-(5-methylpyrazine-2-carboxamido) ethyl] benzene sulphonyl] urea

**Standards:** Glipizide contains not more than the equivalent of 102% and not less than 98 per cent on dry-basis.

**Appearance:** A white crystalline powder

**Melting point:** 208°C-229°C

**Solubility:** Soluble in methylene chloride, sparingly soluble in acetone, practically not soluble in aqua and alcohol. It solibilize in diluted solution of alkali hydroxide.

**pKa:** Glipizide is a weak acid. It has been concluded that it has dissociation constant pKa of 5.9±0.1
2.3.2 Adverse Effects, Treatment and Precautions:

**Adverse Effects:** GI disturbance like heartburn, nausea/vomiting, anorexia diarrhea, and metallic-taste might occur with sulfonylurea and are usually mild and dose dependent. It causes increase in appetite and weight gain may occur. Hypoglycemia occurs with all hypoglycemic agents and may be severe, prolonged and sometimes lethal. Other severe effects may be manifestations of a hypersensitivity reaction. These include leucopenia, aplastic anaemia, cholestatic jaundice, and thrombocytopenia.

**Treatment of Adverse Effects:** In acute-poisoning the abdomen must be vacated by emesis/lavage. Hypo-glycemia must be urgently treated.

**Precautions:** Glipizide used in insulin independent diabetes-mellitus should be avoided in patient having keto-acidosis and in those with severe infection, stress and trauma. Glipizide should not be given in severe destruction of kidney or liver functioning because of increased threat of hypo-glycemia.

2.3.3 Therapeutic Uses: Glipizide is used to control hyperglycemia in type-II diabetes. Usual initial dose in treatment of diabetes is 2.5-5mg daily 3-4times.

2.3.4 Mechanism of Action: Glipizide stimulates the insulin release from the pancreas to acutely lower the blood-glucose levels, this action dependant on function of β-cells in the pancreatic-islets. Exact mechanism of lowering blood glucose by glipizide in long-term administrations is not recognized. Insulin level fasted condition are not increased yet on long term use of glipizide, but the post prandial insulin-response maintained to be improved upon atleast 6-months of therapy.

2.3.5 Pharmacokinetics: Several factors may modify the kinetics of Glipizide some of which are age, fibre intake, presence of autonomic neuropathy, obesity, renal and hepatic insufficiency.

**Absorption:** Glipizide completely absorbed after peroral administration. In the patient with type-2 diabetes Glipizide has absolute bioavailability of 100%. Beginning 2-3 hrs. after ingestion of Glipizide extended release tablet, the drug concentration in plasma steadily increases and reaches utmost concentration in 6-12 hrs after administration. The absorption is delayed with food.
**Distribution:** Glipizide binds to plasma proteins (>99%) and crosses the placenta.

**Metabolism:** Glipizide is metabolized almost completely in the liver.

**Half Life:** Plasma half-life: 2 to 4 hrs.

**Excretion:** Urine (60 to 80%, 91 to 97% as metabolite); fecal (11%)

**Protein Binding:** About 98% binds with plasma proteins. Uses: Glipizide is significant in the treatment of patients with NIDDM, those who have not responded adequately to diet, physical activity, and weight loss.

2.3.6 **Dose:**

**Adults:** Initial: 5mg/day; dose should be adjusted at 2.5 to 5mg everyday increase as resolved by blood-glucose responses at interval of a number of days.

**Immediate-release tablets:** For immediate-release tablets highest suggested once daily dose is 15mg; maximum-recommended total daily dose is 40mg. For extended-release tablets maximum-recommended dose is 20mg.

**Dosage Form:** Tablet: 2.5, 5 and 10 mg

2.3.7 **Packaging and Storage:** Store below 40°C (104°F), preferably between 15°C and 30°C (59 to 86°F) in a well-closed container, when otherwise specified by manufacturer.
Excipients Profile

2.4. Xanthan Gum

![Molecular structure of Xanthan gum](image)

**Fig. No. 18:** Molecular structure of Xanthan gum

2.4.1 General Information

**Synonyms:**

Corn sugar gum, Rhodigel, Keltrol, Xantural, Vanzan NF.

**Structural Formula:**

Xanthan-gum contains repeated units of 5 sugar residue: 2 mannose, 2 glucose and 1 glucuronic acid. Polymers back-bone consist 4 β- D- glucose unit connected at 1\textsuperscript{st} and 4\textsuperscript{th} position, therefore identical in structures to cellulose.

**Biological source:** Xanthan-gum is an anionic poly-saccharide obtained from plants bacteria *Xanthomonas-compestris* by the fermentation process.

**Chemical Name:** Xanthan gum

**Empirical formula and Mol. Weight:**

\((C_{35}H_{49}O_{29})_n\) Approximately 2 \times 106
2.4.2 Description:
Gum Xanthan occur as a white or cream coloured, free flow, odorless, superfine powders.

2.4.3 Typical Properties:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>6.0–8.0 of a 1 %w/v aqueous-solution.</td>
</tr>
<tr>
<td>Freezing point</td>
<td>0°C for a 1 % w/ v water solutions.</td>
</tr>
<tr>
<td>Heats of combustion</td>
<td>14.60 J /g (3.50 cal /g )</td>
</tr>
<tr>
<td>Melting point</td>
<td>Char at 270°C.</td>
</tr>
<tr>
<td>Refractive index</td>
<td>$n_{\text{20 D}} = 1.333$ for a 1 % w/ v water solutions.</td>
</tr>
<tr>
<td>Solubilities</td>
<td>Practically not soluble in ether and ethanol, solubilizes in warm or cold water.</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>1.6000 at 25 °C</td>
</tr>
<tr>
<td>Viscosities (dynamic)</td>
<td>1200–1600 mPas for a 1% w/v aqueous solution at 25°C.</td>
</tr>
</tbody>
</table>

2.4.4 Functional Category:
Suspending agent, viscosity-increasing agent, stabilizing agent.

2.4.5. Applications in Pharmaceuticals:
Xanthan-gum is extensively utilized in peroral formulations, cosmetics and topical-pharmaceutical formulation and food as a stabilizing and suspending agents. In addition it is employed as a thickener and emulsifier.

Xanthan gum furthermore employed to formulate sustained release matrix tablets. Gum Xanthan is included in ophthalmic drug devices that interact with mucin thus helps in extended preservation of the drug device in the pre-corneal region. Current study has uncovered that gum xanthan may be employed as excipients for freeze-drying and spray drying.

2.4.6. Stability and Storage Conditions:
Gum Xanthan is not an unstable substance. Its water solution is stable at broad pH-range (3 to 12) & temperatures of 10 – 60 °C. Solution is as well stable in the existence of salt, bases, acid and enzymes. Xanthan gum must be stocked up in well-closed containers in cool, dry condition.

2.4.7. Incompatibilities:

Gum Xanthan is anionic substance, generally incompatible with cationic surface active agent, some polymer or preservative, it causes precipitate formation. Amphoteric plus Anionic surfactant at concentration above 15% w/v causes precipitate formation of gum xanthan in solutions.

Gum xanthan is incompatible in some tablet film-coatings, oxidizing agents, carboxymethylcellulose sodium, dried aluminum hydroxide gel and some active ingredients such as amitriptyline, tamoxifen and verapamil.

2.5. KARAYA GUM

2.5.1. General Information

Synonyms:
Sterculia, katila, Karaya, kadira, Indian-tragacanth, kadaya, Bassora-tragacanth.

Biological Source:
Karaya-gum, occasionally called as gum Sterculia, it is dried exudates of the Sterculiia Uren Roxb tree. Family: Sterculiaceae. The gum furthermore can be derived from S.vilosa, S. tragacanth.

History:
Gum Karaya has commercial uses from around a century. It was used widely in the earlier 20th-century, it was exploited as an alternative/ adulterants for tragacanth gum. Though, experiments shown that gum-karaya possess specific physio-chemical characteristics which make it further constructive compare to gum-
tragacanth; In addition, karaya-gum is cheaper than tragacanth. Currently it is utilized in a number of product, comprising hair-sprays, cosmetics and lotion etc. [Gauthami, S. and Bhat, 1992]

2.5.2. Physical-properties

The uppermost grades of Gum-Karaya are translucent, whitish and nearly bark free. Inferior grade are brownish to light-yellow and might contains in so far as 3% of insoluble-impurities. The powder form of Gum-Karaya is grayish-white to white. [Ichigawa, M., 1991]

2.5.3. Solubility

Gum Karaya, is doesn’t get solubilised in aqua to form a clear solutions but it form a colloidal solution. The gum karaya powder gets swelled in coldwater to a level so as a 3-4% solution produces a heavy-gel which is consistently smooth. [Iannuccelli sV.et al. 1998]

2.5.4. Viscosity:

The rheology of Gum-Karaya mainly depends on its newness, i.e., how freshly it is collected from tree. Climate condition also affects viscosities of gum-karaya. Its viscosity changes upon long-storage. Gum-Karaya powder shows a reduction in viscosities when stored for more than 6-month. Karaya-Gum sol show sensitivity to alkaline condition and achieve its highest viscosity at pH-8.5.

2.5.5. Chemical Characteristics

Fig. No. 19: Chemical structure of Gum karaya
Karaya-gum is partly acetylated-polysaccharide found as a calcium/magnesium salts. Poly-saccharide components of gum-karaya have a higher molar weights and it comprises galacturonic-acid, glucuronic acid, β-D- galactose, L- rhamnose, & other residue.

It is heavily-acetylated acidic polysaccharide possessing α- D- galactouronic-acid and α- L- rhamnose residues as the major chain with O--4 of acid and O--2 of rhamnose-linkages and the acid was linked by 1, 2-linkage of β- D- galactose or 1, 3 linkage of β-D- glucouronic-acid on side-chains, where 50% of the rhamnose-units carries at O--4 by 1, 4-linkage of β- D- galactose unit [Jain, S.K. et al. 2005]

2.5.6 pH:

pH of 1% GumKaraya solutions is 4.5. Smaller amount of alkalies may be mixed to alter the pH 7 to 8, karaya-gum posess a buffering-action.

2.5.7 Pharmaceutical uses:

Karaya-gum is not absorbed or digested systemically. The gum fundamentally has inertness and does not produce any pharmacological activities. Karaya has a numerous application in the food-industry.

Medicinally, karaya-gum may be effectively used as bulk-laxative, due to absorption of water by gum-particles and it swells up to 60-100 times its original-volume. It acts as bulk-laxative by increasing the gut-contents volume. It is as well employed as adhesives for dental-fixtures. It is also used as demulcent in pastilles to cure sore throat. Karaya-gum coat to the denture used to minimize bacterial-adhesion by 98%.
2.6. Sodium alginate:

2.6.1 General Information

Synonym: Alginic acid.

Biological source:

Sodium-Alginate is the decontaminated carbohydrates obtained by extraction of brown-seaweeds by using of dilute alkalies. It contains not more than 106.0 percent of sodium alginate and not less than 90.8 percent of mean equivalent-weight calculated on dried-basis. Sodium alginate contains principally of the Na-salts of the Alginic-acids, polyuronic-acids containing β- D- manuronic acids residues linked such that the carboxyl-group of all units will be free, whilst the aldehyde-group will have shielding effect by a glycosidic-linkage.

Description: pale yellow, amorphous, free-flowing, fine powder. Obtained as white-yellowish brown filaments, powder or granular form.

2.6.2. Typical Properties:

Solubility: soluble in water. It gradually gets dissolved in water with formation of a viscous-solution; it is insoluble in ether and ethanol. [Benita S. 2005]

2.6.3. Chemistry:

Chemical structure: \((C_6H_7NaO_6)_n\)

Structural formula from Williams, Wedlock and Phillips:

![Chemical structure of Sodium alginate](image)

**Fig. No. 20:** Chemical structure of Sodium alginate
The sequence and number of the Mannuronates and Glucuronates residue as revealed above varies in the naturally obtained alginate-molecules.

**Functional Category:** Suspending-agent, Stabilizing-agent, viscosity modifying agents. Alginates can be used individually prepared adhesive particularly appropriate as food adhesive. It is also available on the textile industry for finishing agent, sizing agents. Also used as stabilizer, emulsifier, thickener and gelling agent.

### 2.6.4 pH:

Sodium alginate is to some extent solubilises in water but in several organic solvents it is insoluble. Sodium alginate powder will get wet when exposed to moisture and combination of the powder and water will make the surface sticky. This stickiness will make the powder become clumps and the dissolve of such clumps will be slower. The content of sugar, starch or protein can decrease the dissolution of it. Monovalent cation such as NaCl could show similar performance when the content is over 0.5%. PH of sodium alginate dissolved in 1% distilled water is about 7.2

### 2.6.5 Stability:

Sodium alginate is hygroscopic and the content of water depends on the relative humidity (RH). Dried sodium alginate is quite stable when stored in well sealed container under temperature no higher than 25 °C. Its solution is stable at pH 5~9. Sodium alginate solution’s stickiness is affected by level of polymerizations and the molar mass. Decrease of stickiness could indicate the decrease of degree of polymerization (DP). High degree of DP is less stable than the product of low DP. Sodium alginate could be hydrolyzed and the hydrolyzation depends on time, temperature and pH. Solution of propylene glycol alginate is stable under room temperature and pH of 3~4; when the pH is lower than 2 or higher than 6, stickiness would decrease quickly even under room temperature.

### 2.6.6 Application in Pharmaceuticals:

- As an odorless gum, alginate is exploited by the food industries as a viscosity-
modifier and as an emulsifying agent.

- A major application for sodium alginate is in reactive dye printing, as thickener for reactive dyestuffs (such as the Procion cotton-reactive dyes) in textile carpet jet-printing and screen-printing. The alginates do not react with these dyes and wash out simply, unlike starch-based thickeners.
- Sodium alginate is a good chelator for pulling radioactive toxins from the body, like iodine-131 and strontium-90 that have taken the place of their non-radioactive counterpart. Alginate as well utilized in enzyme immobilization.
- As a food-additive, sodium-alginate is employed particularly in the gel like food products. E.g. bakers "Chellies" are frequently gelled-alginate "jam."
- These days, it is as well utilized in the biological-experiments for the cell immobilizations to produce significant product such as alcohol and organic-acids.
- Recently, sodium-alginate is employed in molecular-gastronomy at a number of the most excellent restaurant in the world. Sodium-alginate in combination with calciumlactate or analogous compounds to generate sphere of liquids surrounding a thin jelly-membrane. [Bajpai, S.K. and Sharma, S., 2004]

2.7 Sodium bicarbonate

![Fig. No. 21: Chemical structure of Sodium bicarbonate](image)

### 2.7.1 General Information

**Description:** Sodium bicarbonate is white powder, crystalline in nature that is commonly used as a pH buffering agent, a systemic alkalizer, electrolyte replenisher, and in topical cleansing solutions.

**Chemical name:** Sod. Hydrogen carbonates

**Molecular formula:** NaHCO$_3$

**Molecular weight:** 84.00660

**Functional Categories:** Antidiarrheals
2.7.2 Applications:

Neutralizing acid and base:

Each laboratory keeps a container of sodium-bicarbonate in easy-reach, due to its reacting nature with acids and bases. Sodium bicarbonate is amphoteric powder. In addition, as it is comparatively safe in many cases, it is harmless in when used in excessive quantity. Sodium-bicarbonate can be employed to suffocate smaller fires, since heating of sodium-bicarbonate release carbon dioxide. [Baljit Singh et. al., 2010]

Medicinal applications

Sodium-bicarbonate is exploited in an aqueous-solution to reduce acidity when administered by oral route for treatment of acid-indigestion and heartburns. It might as well used in the treatment of severe metabolic-acidosis such as renal-tubular acidosis and chronic kidney failure. It might as well use in urinary-alkalinization to treat of aspirin overdoses and uric-acid renal stone. Sodium bicarbonate is employed as the medical component in gripe-water for infant. Sodium bicarbonate is employed in the form of aqueous I.V. solutions occasionally used in the case of acidosis or when there are inadequate Na or HCO$_3$ ions in the plasma.

It is also used to treat the hyper-kalemia. NaHCO$_3$ can induce alkalosis; hence it is occasionally used in the treatment of aspirin overdose. For proper absorption of aspirin, it requires an acidic-environment, and the aspirin absorption gets reduced in the basic-environment in the case of an overdose. Sodium bicarbonate may be used topically in the form of paste in 3:1 ratio with water to relieve insect bites.

Cleansing aid

Sodium bicarbonate paste may be used effectively in scrubbing and cleansing. Sodium bicarbonate is usually added to washing-machines as a substitute for softeners and as well used for removal of odor from clothing. It is also effectively used in removal of tea/coffee stain from cups. [Baljit Singh et. al., 2010]
2.8. HydroxypropylMethylCellulose [HPMC] K100-M, K15-M, K4-M,

Fig. No. 22: General chemical structure of HPMC

2.8.1 General Information

Non-proprietary Name :  
BP: Hypromellose
JP: Hypromellose
PhEur: Hypromellose
USP: Hypromelloses

Synonym :  
Hydroxy propyl methyl cellulose; HPMC; Hypromellose; Methocel; Metolose.

Chemical-Name :  
CelluloseHydroxy propyl methyl ether.

Molecular Weight :  
Molecular weight is 10000–1500 000.

Functional Category :  
Bio adhesive material; controlled-release agent; extended-release agent; film-forming agent; modified-release agent; mucoadhesive; release-modifying agent; solubilising-agent; thickening agent; stabilizing-agent; sustained-release polymer.

Description :  
HPMC are a tasteless and odorless, creamy white to white granular or fibrous powders.
2.8.2 Typical Properties:

**pH** : 5.0–8.0 for a 2 %w/w aqueous solution.

**Melting point** : Browns at 190–200°C; chars at 225–230°C Glass transition

Temperature is 170–180°C.

**Solubility** : Practically not soluble in hot water, chloroform, ether and ethanol (95%), Solubilizes in cold-water, with formation of a viscous colloidal solution; but dissolves in mixture of ethanol & dichloromethane, mixture of methanol & dichloromethane, and mixture of water & alcohol.

**Specific gravity** : 1.26 at 25°C.

**Viscosity (dynamic)** : HPMC K4 M has Nominal viscosity (mPas) 4 for 1 % w/v water solutions at room temp.

HPMC K 15 M has Nominal viscosity (mPas) 15 for 1 % w/v water solutions at room temp.

HPMC K 100 M has Nominal viscosity (mPas) 100 for 1% w/v water solutions at room temp.

**Incompatibilities** : It is incompatible with some oxidizing agent. As it is non-ionic, Hypromelose will not form complexes in the company of metallic salt or ion organic to shape non soluble precipitate.

2.8.3 Stability and Storage Conditions:

- Hypromellose in powdered form is sturdy substance, though it is hygroscopic subsequent to drying. Its solution is stable at pH 3-11.

- Hypromellose undergo a reversible sol to gel transformations on application of heat and freezing.
• Gelation temperature is 50 to 90°C, depends on the grades and concentrations of materials.

2.8.4 Safety:

• It is broadly utilized as an excipient in ophthalmic, peroral, nasal and pharmaceuticals for topical use.
• Hypromellose is employed as well in commonly in cosmetic and food-product.
• It is usually considered as a non-toxic and nonirritating substance, though too much peroral use can show laxative effects. (16) In fact, high dosages of Hypromellose are being investigated for treating various metabolic syndromes.
• LD-50 (mice, I.P.): 5g /kg. LD-50 (rats, I.P.): 5.2g /kg.

2.8.5. Applications in Pharmaceuticals:

• It is extensively utilized in topical, ophthalmic, nasal, and peroral pharmaceuticals formulation.

• According to the viscosity-grades, concentration of 2 to 20%w/w was employed as film forming solution to film-coat tablets.

• Lesser viscosity-grade of HPMC is used in aqueous-film coating solutions, while higher-viscosity grades are used with organic solvents.

• It is also useful as a thickening-agent and suspending-agent in transdermal formulation.

• It is also used commercially in liquid nasal formulations at a concentration of 0.1%.

• It is used as an emulsifying agent, stabilizing-agent, suspending-agent and in topical gel and ointment.

2.9. Starch 1500:
2.9.1 General Information

Starch-1500 is a distinctive pharmaceuticals additive having numerous characteristics in a solitary material. Starch-1500 executes the various functions such as a disintegrant, flow-aid, binder and also has lubricant-property. Starch 1500 is exceptionally multipurpose and efficient in a number of process/methods of solid peroral drug delivery systems, like wet granulation, direct-compression, encapsulation, dry granulation and roller compactions. Starch-1500 is predominantly effectual with moisture-sensitive drugs and low-dose application and exhibit synergism. It enhances utility of further frequently utilized excipient in formulation.

It also provides exceptional variety of function and supple performances in a range of application.

Starch-1500 curtails method and materials cost by eliminating or minimizing:

- Polymer binder
- Superdisintegrant
- Use of higher amount of lubricant and glidant
- Manufacturing-steps

2.9.2. Manufacturing Process:
Starch-1500 is a fractionally pre-gelatinized starch (maize) produced utterly for the pharmaceuticals in devoted c-GMP facility. The procedure involve substantial modifications of the starches (no use of surfactants or chemical additives), ensuing the collective advantages of the insoluble and soluble functionalities of Starch1500.

Fractional pregelatinization of Starch1500 provides it an exceptional characteristic. The procedure consequences increased particle size, partial-solubility, superior flowability and compressibility compare to other “starches.” Starch-1500 possesses characteristics of both-native and completely gelatinised starch making it functional as a binding agent and a disintegrating agent in formulation prepared by wet granulation.

Starch 1500 is exceptionally multipurpose and efficient in a number of process methods of solid peroral drug delivery systems, like wet granulation, direct-compression, encapsulation, dry granulation and roller compactions. Starch-1500 is predominantly effectual with moisture-sensitive drugs and low-dose application and exhibit synergism. It enhances utility of further frequently utilized excipient in formulation.

The Starch-1500 when mixed with cold-water it produces viscous-slurry or, alternatively, could be kept to the granulator-bowl directly and water could be used for granulation.

2.9.3 Applications:

**Binding agent**

- It can be used as wet as well as dry binding agent, which allows flexibility in method.
- Improves the functionality of other-excipient used to make tablet with admirable-hardness and low-friability.
- Reduction in manufacture cost related with the distinctive binding solution preparations.

**Disintegrating agent**
• It acts as useful disintegrating agent and avoids the use of expensive super-disintegrants that reduces film-coating qualities.

Flow-aid

• Starch 1500 has outstanding flowing property, ensuring drug-content and weight-uniformity of tablet and capsule.

Lubricants

• It has Self lubricating ability, which eradicates negative-effect on dissolutions or film-coating qualities observed with another lubricant.

It also provides exceptional variety of function and supple performances in a range of application.