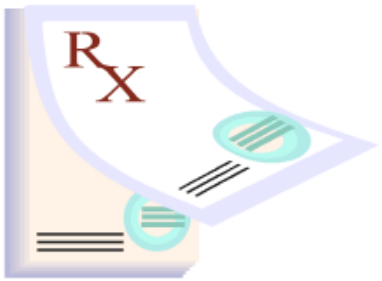
# Appendix-I



## EXCIPIENTS PROFILE

### A. ASPARTAME [1]

**Nonproprietary Names:** BP: Aspartame

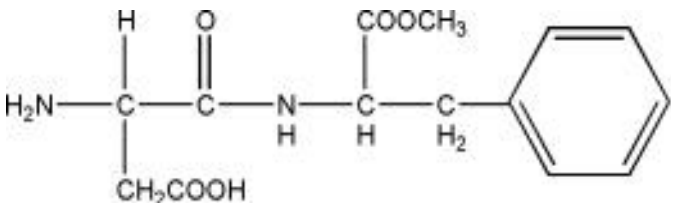
**Synonyms:** 3-amino-*N* (methoxycarbonylphenethyl) succinamic acid; APM; aspartyl phenylamine methyl ester; NutraSweet; Pal Sweet; Pal Sweet Diet.

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

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

**Molecular Weight:** 294.31

**Structural Formula:**




**Functional Category:** Sweetening agent.

**Applications in Pharmaceutical Formulation or Technology:** Aspartame is used as an intense sweetening agent in beverage products, food products, and table-top sweeteners, and in pharmaceutical preparations including tablets, powder mixes, and vitamin preparations. It enhances flavor systems and can be used to mask some unpleasant taste characteristics; the approximate sweetening power is 180–200 times that of sucrose.

Unlike some other intense sweeteners, aspartame is metabolized in the body and consequently has some nutritive value: 1 g provides approximately 17 kJ (4 kcal). However, in practice, the small quantity of aspartame consumed provides a minimal nutritive effect. Therapeutically, aspartame has also been used in the treatment of sickle cell anemia.

**Description:** Aspartame occurs as an off white, almost odorless crystalline powder with an intensely sweet taste.

**Melting point:** 246–247°C

**Solubility:** slightly soluble in ethanol (95%); sparingly soluble in water. At 20°C the solubility is 1% w/v at the isoelectric point (pH 5.2). Solubility increases at higher temperature and at more acidic pH, e.g., at pH 2 and 20°C solubility is 10% w/v.

**Stability and Storage Conditions:** Aspartame is stable in dry conditions. In the presence of moisture, hydrolysis occurs to form the degradation products L-aspartyl-L-phenylalanine and 3-benzyl-6-carboxymethyl-2,5- diketopiperazine. A third-degradation product is also known, L-aspartyl-L-phenylalanine methyl ester.

**B. CELPHERE [2]**

**Synonym:** Microcrystalline Cellulose Spheres USP/NF, EP, JPE

Celphere is a 100 percent pure microcrystalline cellulose sphere which is highly spherical and uniform in its particle size distribution, enabling greater accuracy and consistency in drug layering and coating. Different grades of celpheres with their particle size are mentioned in Table 2.3.

This product exhibits high mechanical strength and low friability allowing it to withstand the rigors of fluidized-bed or wurster coating process. Celphere is insoluble, yet it absorbs water during processing, thereby reducing particle agglomeration even at high spray rates. During dissolution it avoids film deformation or rupturing under stress. It has low chemical reactivity and hence can be freely used to layer high dose, moisture sensitive and potent actives.

**Table 1: Different grades of Celpheres with their particle size**

| Grade | Particle size range (µm) | Applications |
|---|---|---|
| Celphere CP-102 | 106 - 212 | Used as a spherical seed core for drug layering, film coating and also for manufacturing sustained-release or taste masked granules. |
| Celphere CP-203 | 150 - 300 | |
| Celphere CP-305 | 300 - 500 | |
| Celphere CP-507 | 500 - 710 | |
| Celphere CP-708 | 710 - 850 | |

**C. COLLOIDAL SILICON DIOXIDE [1]**

**Nonproprietary Names:** BP: Colloidal anhydrous silica

**Synonyms:** Aerosil; Cab-O-Sil; Cab-O-Sil M-5P; colloidal silica; fumed silica; light anhydrous silicic acid; silicic anhydride; silicon dioxide fumed.

**Empirical Formula:** $SiO_2$

**Molecular Weight:** 60.08

**Functional Category:** Adsorbent; anticaking agent; emulsion stabilizer; glidant; suspending agent; tablet disintegrant; thermal stabilizer; viscosity-increasing agent.

**Applications in Pharmaceutical Formulation or Technology:** Colloidal silicon dioxide is widely used in pharmaceuticals, cosmetics, and food products (Table 2.6). Its small particle size and large specific surface area give it desirable flow characteristics that are exploited to improve the flow properties of dry powders in a number of processes such as tableting.

**Table 2: Uses of colloidal silicon dioxide**

| **Uses** | **Concentration** |
|---|---|
| Aerosols | 0.5-2.0 |
| Emulsion stabilizers | 1.0-5.0 |
| Glidant | 0.1-0.5 |

Colloidal silicon dioxide is also used to stabilize emulsions and as a thixotropic thickening and suspending agent in gels and semisolid preparations. With other ingredients of similar refractive index, transparent gels may be formed. The degree of viscosity increase depends on the polarity of the liquid (polar liquids generally require a greater concentration of colloidal silicon dioxide than nonpolar liquids). Viscosity is largely independent of temperature. However, changes to the pH of a system may affect the viscosity.

Colloidal silicon dioxide is also used as a tablet disintegrant and as an adsorbent dispersing agent for liquids in powders. Colloidal silicon dioxide is frequently added to suppository formulations containing lipophilic excipients to increase viscosity, prevent sedimentation during molding, and decrease the release rate. Colloidal silicone dioxide is also used as an adsorbent during the preparation of wax microspheres; as a thickening agent for topical preparations; and has been used to aid the freeze-drying of nanocapsules and nanosphere suspensions.

**Description:** Colloidal silicon dioxide is submicroscopic fumed silica with a particle size of about 15 nm. It is a light, loose, bluish-white-colored, odorless, tasteless, nongritty amorphous powder.

**Stability and Storage Conditions:** Colloidal silicon dioxide is hygroscopic but adsorbs large quantities of water without liquefying. When used in aqueous systems at a pH 0–7.5, colloidal silicon dioxide is effective in increasing the viscosity of a system. However, at a pH greater than 7.5 the viscosity-increasing properties of colloidal silicon dioxide are reduced; and at a pH greater than 10.7 this ability is lost entirely since the silicon dioxide dissolves to form silicates.

Colloidal silicon dioxide powder should be stored in a well-closed container. Some grades of colloidal silicon dioxide have hydrophobic surface treatments that greatly minimize their hygroscopicity.

**D. CROSCARMELLOSE SODIUM [1]**

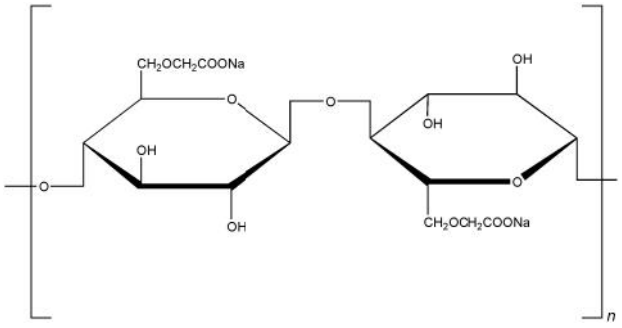
**Nonproprietary Names:** BP: Croscarmellose sodium

**Synonyms:** Ac-Di-Sol; cross-linked carboxymethylcellulose sodium; Explocel; modified cellulose gum

**Chemical Name:** Cellulose, carboxymethyl ether, sodium salt, crosslinked

**Empirical Formula:** Cross-linked polymer of carboxymethylcellulose sodium

**Structural Formula:**




**Functional Category:** Tablet and capsule disintegrant.

**Applications in Pharmaceutical Formulation or Technology:** Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules, tablets and

granules.In tablet formulations, croscarmellose sodium may be used in both direct-compression and wet-granulation processes. When used in wet granulations, the croscarmellose sodium should be added in both the wet and dry stages of the process (intra- and extragranularly) so that the wicking and swelling ability of the disintegrant is best utilized. Croscarmellose sodium at concentrations up to 5% w/w may be used as a tablet disintegrant, although normally 2% w/w is used in tablets prepared by direct compression and 3% w/w in tablets prepared by a wet-granulation process.

**Description:** Croscarmellose sodium occurs as an odorless, white or grayish-white powder.

**Solubility:** insoluble in water, although croscarmellose sodium rapidly swells to 4–8 times its original volume on contact with water. Practically insoluble in acetone, ethanol and toluene.

**Stability and Storage Conditions:** Croscarmellose sodium is a stable though hygroscopic material. A model tablet formulation prepared by direct compression, with croscarmellose sodium as a disintegrant, showed no significant difference in drug dissolution after storage at 30°C for 14 months. Croscarmellose sodium should be stored in a well-closed container in a cool, dry place.

**E. CROSPOVIDONE [1]**

**Nonproprietary Names:** BP: Crospovidone

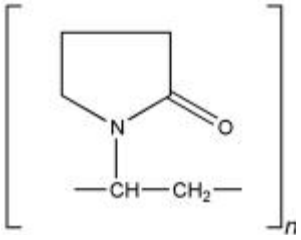
**Synonyms:** Crosslinked povidone; E1202; Kollidon CL; Kollidon CL-M; Polyplasdone XL; Polyplasdone XL-10; polyvinylpolypyrrolidone; PVPP; 1-vinyl-2-pyrrolidinone homopolymer.

**Chemical Name:** 1-Ethenyl-2-pyrrolidinone homopolymer

**Empirical Formula:** $(C_6H_9NO)_n$

**Molecular Weight:** >1,000,000 (The USPNF 23 describes crospovidone as a water-insoluble synthetic crosslinked homopolymer of *N*-vinyl-2-pyrrolidinone. An exact determination of the molecular weight has not been established because of the insolubility of the material.)

**Structural Formula:**




**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. Studies suggest that the particle size of 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. Density of different commercial grades of crospovidone is described in table 2.5.

**Table 3: Density values of commercial grades of crospovidone**

| **Commercial grade** | **Density (bulk) g/cm$^3$** | **Density (tapped) g/cm$^3$** |
|---|---|---|
| Kollidon CL | 0.3–0.4 | 0.4–0.5 |
| Kollidon CL-M | 0.15–0.25 | 0.3–0.5 |
| Polyplasdone XL | 0.213 | 0.273 |
| Polyplasdone XL-10 | 0.323 | 0.461 |

## F. HYDROXY PROPYL CELLULOSE (KLUCEL EXF) [1]

**Nonproprietary Names:** Hydroxypropylcellulose

**Synonyms:** Cellulose, hydroxypropyl ether; E463; hyprolose; *Klucel*; *Methocel*; *Nisso HPC*; oxypropylated cellulose.

**Functional Category:** Coating agent; emulsifying agent; stabilizing agent; suspending agent; tablet binder; thickening agent; viscosity-increasing agent.

**Applications in Pharmaceutical Formulation or Technology:** In oral products, hydroxypropyl cellulose is primarily used in tableting as a binder, filmcoating, and extended-release-matrix former. Concentrations of hydroxypropyl cellulose of 2–6% w/w may be used as a binder in either wet-granulation or dry, direct-compression tableting processes. Concentrations of 15–35% w/w of hydroxypropyl cellulose may be used to produce tablets with an extended drug release. The release rate of a drug increases with decreasing viscosity of hydroxypropyl cellulose. The addition of an anionic surfactant similarly increases the viscosity of hydroxypropyl cellulose and hence decreases the release rate of a drug. Typically, a 5% w/w solution of hydroxypropyl cellulose may be used to film coat tablets. Hydroxypropyl cellulose is also used in microencapsulation processes and as a thickening agent.

**Description:** Hydroxypropyl cellulose is a white to slightly yellow-colored, odorless and tasteless powder.

**Melting point: S**oftens at 130°C; chars at 260–275°C.

**Moisture content:** Hydroxypropyl cellulose absorbs moisture from the atmosphere; the amount of water absorbed depends upon the initial moisture content and the temperature and relative humidity of the surrounding air. Typical equilibrium moisture content values at 25°C are 4% w/w at 50% relative humidity and 12% w/w at 84% relative humidity.

**Stability and Storage Conditions:** Hydroxypropyl cellulose powder is a stable material, although it is hygroscopic after drying.

Aqueous solutions of hydroxypropyl cellulose are stable at pH 6.0–8.0, with the viscosity of solutions being relatively unaffected. The rate of hydrolysis increases with increasing temperature and hydrogen ion concentration. At high pH, alkali-catalyzed oxidation may

degrade the polymer and result in a decrease in viscosity of solutions. This degradation can occur owing to the presence of dissolved oxygen or oxidizing agents in a solution.

Increasing temperature causes the viscosity of aqueous solutions to decrease gradually until the viscosity drops suddenly at about 45°C owing to the limited solubility of hydroxypropyl cellulose. Solutions of hydroxypropyl cellulose in organic solvents do not generally require preservatives. Ultraviolet light will also degrade hydroxypropyl cellulose and aqueous solutions may therefore decrease slightly in viscosity if exposed to light for several months. Aqueous hydroxypropyl cellulose solutions have optimum stability when the pH is maintained at 6.0–8.0, and also when the solution is protected from light, heat, and the action of microorganisms. Hydroxypropyl cellulose powder should be stored in a well-closed container in a cool, dry place.

## G. HYDROXY PROPYL METHYL CELLULOSE [1]

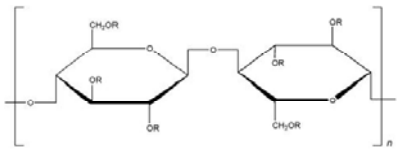
**Nonproprietary Names:** BP: Hypromellose

**Synonyms:** Benecel MHPC; E464; Methocel; methylcellulose propylene glycol ether; methyl hydroxypropylcellulose; Metolose; Tylopur.

**Chemical Name:** Cellulose hydroxypropyl methyl ether

**Empirical Formula and Molecular Weight:** The PhEur 2005 describes hypromellose as 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, in mPa s, of a 2% w/w aqueous solution at 20°C. Hypromellose defined in the USP 28 specifies the substitution type by appending a four-digit number to the nonproprietary name: e.g., hypromellose 1828. The first two digits refer to the approximate percentage content of the methoxy group ($OCH_3$). The second two digits refer to the approximate percentage content of the hydroxypropoxy group ($OCH_2CH(OH)CH_3$), calculated on a dried basis. It contains methoxy and hydroxypropoxy groups conforming to the limits for the types of hypromellose stated in Table I. Molecular weight is approximately 10 000–1 500 000. The JP 2001 includes three separate monographs for hypromellose: hydroxypropylmethylcellulose 2208, 2906, and 2910, respectively.

**Structural Formula:**



Where, R is H, $CH_3$, or $CH_3CH(OH)CH_2$

**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:** In oral products, hypromellose is primarily used as a tablet binder, in film-coating, and as a matrix for use in extended-release tablet formulations. Concentrations between 2% and 5% w/w may be used as a binder in either wet- or dry-granulation processes. 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-coat tablets. Lower-viscosity grades are used in aqueous film-coating solutions, while higher-viscosity grades are used with organic solvents.

Hypromellose is also used as an emulsifier, suspending agent, and stabilizing agent in topical gels and ointments. As a protective colloid, it can prevent droplets and particles from coalescing or agglomerating, thus inhibiting the formation of sediments.

**Description:** Hypromellose is an odorless and tasteless, white or creamy-white fibrous or granular powder.

**Melting point:** Browns at 190–200°C; chars at 225–230°C. Glass transition temperature is 170–180°C.

**Solubility:** Soluble in cold water, forming a viscous colloidal solution; practically insoluble in chloroform, ethanol (95%), and ether, but soluble in mixtures of ethanol and dichloromethane, mixtures of methanol and dichloromethane, and mixtures of water and alcohol. Certain grades of hypromellose are soluble in aqueous acetone solutions, mixtures of dichloromethane and propan-2-ol, and other organic solvents.

**Stability and Storage Conditions:** Hypromellose 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. Hypromellose undergoes a reversible sol–gel transformation upon heating and cooling, respectively. The gel point is 50–90°C, depending upon the grade and concentration of material.

Aqueous solutions are comparatively enzyme-resistant, providing good viscosity stability during long-term storage. However, aqueous solutions are liable to microbial spoilage and should be preserved with an antimicrobial preservative: when hypromellose is used as a viscosity-increasing agent in ophthalmic solutions, benzalkonium chloride is commonly used as the preservative. Aqueous solutions may also be sterilized by autoclaving; the coagulated polymer must be redispersed on cooling by shaking. Hypromellose powder should be stored in a well-closed container, in a cool, dry place.

**H. MANNITOL (PEARLITOL SD 200) [1]**

**Nonproprietary Names:** USP: Mannitol

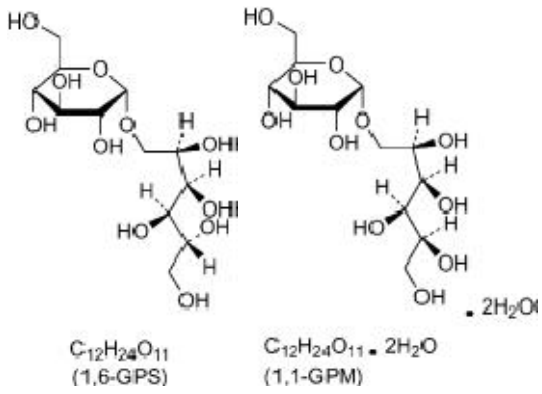
**Synonyms:** Cordycepic acid, manna sugar; D-mannite, mannite, Mannogem, Pearlitol.

**Chemical Name:** D-Mannitol

**Empirical Formula:** $C_{12}H_{24}O_{11}$ (for anhydrous); $C_{12}H_{24}O_{11}\cdot 2H_2O$ (for dihydrate)

**Molecular Weight:** 344.32 (for anhydrous); 380.32 (for dihydrate)

**Structural Formula:**




**Functional Category:** Diluent; diluent for lyphilized preparations; sweetening agent; tablet and capsule diluent; tonicity agent.

**Applications in Pharmaceutical Formulation or Technology:** Mannitol is widely used in pharmaceutical formulations and food products. In pharmaceutical preparations it is primarily used as a diluent (10–90% w/w) in tablet formulations, where it is of particular value since it is not hygroscopic and may thus be used with moisture-sensitive active ingredients. Mannitol may be used in direct-compression tablet applications, for which the granular and spray-dried forms are available, or in wet granulations. Granulations containing mannitol have the advantage of being dried easily. Specific tablet applications include antacid preparations, glyceryl trinitrate tablets, and vitamin preparations. Mannitol is commonly used as an excipient in the manufacture of chewable tablet formulations because of its negative heat of solution, sweetness, and 'mouth feel'.

Mannitol has also been used to prevent thickening in aqueous antacid suspensions of aluminum hydroxide (<7% w/v). It has been suggested as a plasticizer in soft-gelatin capsules, as a component of sustained-release tablet formulations, and as a carrier in dry powder inhalers. It is also used as a diluent in rapidly dispersing oral dosage forms. It is used in food applications as a bulking agent.

**Description:** Mannitol is D-mannitol. It is a hexahydric alcohol related to mannose and is isomeric with sorbitol. Mannitol occurs as a white, odorless, crystalline powder, or free-flowing granules. It has a sweet taste, approximately as sweet as glucose and half as sweet as sucrose, and imparts a cooling sensation in the mouth. Microscopically, it appears as orthorhombic needles when crystallized from alcohol.

**Stability and Storage Conditions:** Mannitol is stable in the dry state and in aqueous solutions. Solutions may be sterilized by filtration or by autoclaving and if necessary may be autoclaved repeatedly with no adverse physical or chemical effects. In solution, mannitol is not attacked by cold, dilute acids or alkalis, nor by atmospheric oxygen in the absence of catalysts. Mannitol does not undergo Maillard reactions. The bulk material should be stored in a well-closed container in a cool, dry place.

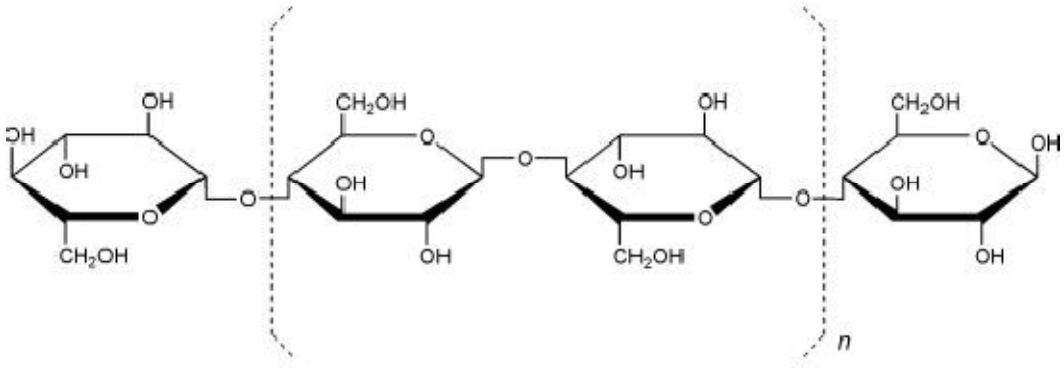
## I. MICROCRYSTALLINE CELLULOSE [1]

**Nonproprietary Names:** BP: Microcrystalline cellulose

**Synonyms:** Avicel PH; Celex; cellulose gel; Celphere; Ceolus KG; crystalline cellulose; E460; Emcocel; Ethispheres; Fibrocel; Pharmacel; Tabulose; Vivapur.

**Chemical Name:** Cellulose

**Structural Formula:**




**Functional Category:** Adsorbent; suspending agent; tablet and capsule diluent; tablet disintegrant.

**Applications in Pharmaceutical Formulation or Technology:** Microcrystalline cellulose is widely used in pharmaceuticals, primarily as a binder/diluent in oral tablet and capsule formulations where it is used in both wet-granulation and direct compression processes. In addition to its use as a binder/diluent, microcrystalline cellulose also has some lubricant and disintegrant properties that make it useful in tabletting.

**Table 4: Uses of microcrystalline cellulose**

| **Use** | **Concentration (%)** |
|---|---|
| Adsorbent | 20–90 |
| Antiadherent | 5–20 |
| Capsule binder/diluent | 20–90 |
| Tablet disintegrant | 5–15 |
| Tablet binder/diluents | 20–90 |

**Description:** Microcrystalline cellulose is a 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 have different properties and applications.

**Melting point:** Chars at 260–270 °C.

**Stability and Storage Conditions:** Microcrystalline cellulose is a stable though hygroscopic material. The bulk material should be stored in a well-closed container in a cool, dry place.

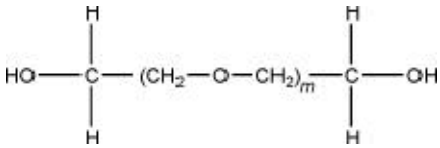
## J. POLY ETHYLENE GLYCOL 6000 [1]

**Nonproprietary Names:** BP: Macrogols; USPNF: Polyethylene glycol

**Synonyms:** Carbowax; Carbowax Sentry; Lipoxol; Lutrol E; PEG; Pluriol E; polyoxyethylene glycol.

**Chemical Name:** Hydro -hydroxypoly(oxy-1,2-ethanediyl)

**Structural Formula:**



**Functional Category:** Ointment base; plasticizer; solvent; suppository base; tablet and capsule lubricant

**Applications in Pharmaceutical Formulation or Technology:** Polyethylene glycols (PEGs) are widely used in a variety of pharmaceutical formulations including parenteral, topical, ophthalmic, oral, and rectal preparations. Aqueous polyethylene glycol solutions can be used either as suspending agents or to adjust the viscosity and consistency of other suspending vehicles. When used in conjunction with other emulsifiers, polyethylene glycols can act as emulsion stabilizers.

In solid-dosage formulations, higher-molecular-weight polyethylene glycols can enhance the effectiveness of tablet binders and impart plasticity to granules. However, they have only limited binding action when used alone, and can prolong disintegration if present in concentrations greater than 5% w/w.

**Description:** Polyethylene glycol as being an addition polymer of ethylene oxide and water. Polyethylene glycol grades 200–600 are liquids; grades 1000 and above are solids at ambient temperatures. Grades of PEG 6000 and above are available as free-flowing milled powders.

**Typical Properties:**

**Density:** 1.15–1.21 g/cm3 at 25°C for solid PEGs.

**Melting point:** 55–63°C for PEG 6000

**Dynamic Viscosity:** 200–270 cps

**Moisture content:** Solid grades, e.g. PEG 4000 and above, are not hygroscopic

**Solubility:** All grades of polyethylene glycol are soluble in water and miscible in all proportions with other polyethylene glycols. Solid polyethylene glycols are soluble in acetone, dichloromethane, ethanol (95%), and methanol; they are slightly soluble in aliphatic hydrocarbons and ether, but insoluble in fats, fixed oils, and mineral oil.

**Stability and Storage Conditions:** Polyethylene glycols are chemically stable in air and in solution. Polyethylene glycols do not support microbial growth, and they do not become rancid.

Polyethylene glycols should be stored in well-closed containers in a cool, dry place.

## K. POLYMETHACRYLATES [1]

**Synonyms:** Acryl-EZE; Eastacryl 30D; Eudragit; Kollicoat MAE 30 D; Kollicoat MAE 30 DP

**Chemical Name:**

Eudragit RL 100: Poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) 1 : 2 : 0.2;

Eudragit RS 100: Poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) 1 : 2 : 0.1;

Eudragit EPO: Poly(butyl methacrylate, (2-dimethylaminoethyl) methacrylate, methyl methacrylate) 1 : 2 : 1

**Applications in Pharmaceutical Formulation or Technology:** Polymethacrylates are primarily used in oral capsule and tablet formulations as film-coating agents. Depending on the type of polymer used, films of different solubility characteristics can be produced.

- Eudragit RL 100: Sustained release
- Eudragit RS 100: Sustained release
- Eudragit EPO: Film coating

- **Eudragit RL and Eudragit RS,** also referred to as ammonio methacrylate copolymers, synthesized from acrylic acid and methacrylic acid esters, with Eudragit RL (Type A) having 10% of functional quaternary ammonium groups and Eudragit RS (Type B) having 5% of functional quaternary ammonium groups. The ammonium groups are present as salts and give rise to pH-independent permeability of the polymers. Both polymers are water-insoluble, and films prepared from Eudragit RL are freely permeable to water, whereas, films prepared from Eudragit RS are only slightly permeable to water. Solutions are colorless or slightly yellow in color, and may be clear or slightly turbid; they have an odor characteristic of the solvents. Solvent-free granules (Eudragit RL 100 and Eudragit RS 100) contain 697% of the dried weight content of the polymer.

- **Eudragit E** is cationic polymer based on dimethylaminoethyl methacrylate and other neutral methacrylic acid esters. It is soluble in gastric fluid as well as in weakly acidic buffer solutions. It is light yellow in color with the characteristic odor of the solvents. Solvent-free granules contain ˜{98% dried weight content of Eudragit E.
- **Eudragit EPO** is a white free-flowing powder with at least 95% of dry polymer.

**Stability and Storage Conditions:** Dry powder polymer forms are stable at temperatures less than 30°C. Above this temperature, powders tend to form clumps, although this does not affect the quality of the substance and the clumps can readily be broken up. Dry powders are stable for at least 3 years if stored in a tightly closed container at less than 30°C.

Dispersions are sensitive to extreme temperatures and phase separation occurs below 0°C. Dispersions should therefore be stored at temperatures between 5 and 25°C and are stable for at least 18 months after shipping from the manufacturer's warehouse if stored in a tightly closed container at the above conditions (12).

## L. SILICIFIED MICROCRYSTALLINE CELLULOSE [1]

**Synonym:** PROSOLV SMCC HD90

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

**Applications in Pharmaceutical Formulation or Technology:** Silicified microcrystalline cellulose is used as a filler in the formulation of capsules and tablets. It

has improved compaction properties in both wet granulation and direct compression compared to conventional microcrystalline cellulose. Silicified microcrystalline cellulose was specifically developed to address the loss of compaction that occurs with microcrystalline cellulose after wet granulation.

**Description:** Silicified microcrystalline cellulose (PROSOLV® SMCC) is a synergistic, intimate physical mixture of two components: microcrystalline cellulose and colloidal silicon dioxide. Silicified microcrystalline cellulose contains 2% w/w colloidal silicon dioxide.

A high functionality and multifunctional excipient, it requires less complex processing, has high inherent functionality, and passes that functionality on to the drug formulation.

PROSOLV® SMCC is unique in that it imparts both optimum compaction and superior flow to formulations. It also exhibits both brittle fracture and plastic deformation characteristics, leading to superior binding properties. The production process of PROSOLV® SMCC leads to homogenous and much finer CSD particle size distribution. This result in a five-fold specific surface area increase, as well as in a 30-50% compaction increase compared to traditional MCC. The increased surface area enables superior flow and increased compaction and results in improved content uniformity and stability in the formulation [3].

When used for direct compression, PROSOLV® SMCC can replace granulations, while significantly reducing the number of required excipients and use levels. PROSOLV® SMCC formulations produce distinctive, uniform, and cost effective tablets. Different grades of PROSOLV® SMCC are available (Table 2.4). PROSOLV® SMCC offers Excellent compactibility, High intrinsic flow, Enhanced lubrication efficiency, Improved blending properties, Superior binding properties and increased production capacity.

**TABLE 5: Different grades of PROSOLV® SMCC**

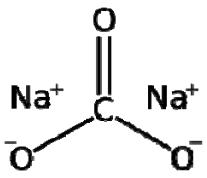
| Grade | Average Particle Size by Laser Diffraction (µm) | Bulk Density (g/mL) | Main Application |
|---|---|---|---|
| PROSOLV® SMCC 50 | 65 | 0.25 – 0.37 | Formulas in which optimal compaction and decent flow is required. |
| PROSOLV® SMCC 50 LD | 50 | 0.20 – 0.30 | Best in class binders. |
| PROSOLV® SMCC 90 | 125 | 0.25 – 0.37 | Formulas in which a balance of flow and compaction is required. |
| PROSOLV® SMCC HD 90 | 125 | 0.38 – 0.50 | Formulas in which optimal flow and consolidation is required. This grade shows the best disintegration times. *Low moisture grade available on request. |
| PROSOLV® SMCC 90 LM | 125 | 0.27 – 0.39 | Equivalent to quality of PROSOLV® SMCC 90, but with lower moisture content (< 3%) |

**M. SODIUM CARBONATE**

**Nonproprietary Names:** USP: Disodium carbonate

**Synonyms:** Soda ash, Washing soda, Soda crystals

**Structural Formula:**




**Functional Category:** Sodium carbonate is a food additive (E500) used as an acidity regulator, anticaking agent, raising agent, and stabilizer.

**Solubility:** It is freely soluble in water and insoluble in ethanol.

**Applications in Pharmaceutical Formulation or Technology:** It acts as an alkali because when dissolved in water, it dissociates into the weak acid: carbonic acid and the strong alkali; sodium hydroxide.

**Description:** Sodium carbonate, $Na_2CO_3$, occurs as colorless crystals or as a white, granular or crystalline powder. It is the water-soluble sodium salt of carbonic acid. It most commonly occurs as a crystalline heptahydrate, which readily effloresces to form a white powder, the monohydrate.

**Melting point:** 851 °C (anhydrous)

**Stability and Storage Conditions:** Stable at ordinary temperature and atmospheric conditions; dries out somewhat in warm, dry air or above 50 ° C.

**N. SODIUM STEARYL FUMARATE [1]**

**Nonproprietary Names:** BP: Sodium stearyl fumarate

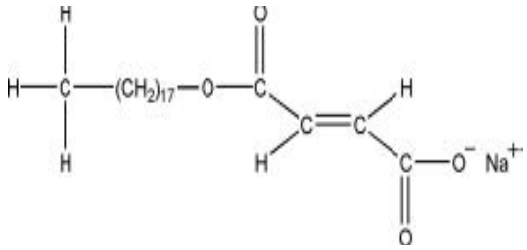
**Synonyms:** Fumaric acid, octadecyl ester, sodium salt; *Pruv*; sodium monostearyl fumarate.

**Chemical Name:** 2-Butenedioic acid, monooctadecyl ester, sodium salt

**Empirical Formula:** $C_{22}H_{39}NaO_4$

**Molecular Weight:** 390.5

**Structural Formula:**



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

**Applications in Pharmaceutical Formulation or Technology:** Sodium stearyl fumarate is used as a lubricant in capsule and tablet formulations at 0.5–2.0%w/w concentration. It is also used in certain food applications.

**Description:** Sodium stearyl fumarate is a fine, white powder with agglomerates of flat, circular-shaped particles.

**Melting point:** 224–245°C (with decomposition)

**Solubility:** Practically insoluble in acetone, chloroform, ethanol, methanol.

**Stability and Storage Conditions:** At ambient temperature, sodium stearyl fumarate is stable for up to 3 years when stored in amber glass bottles with polyethylene screw caps.

The bulk material should be stored in a well-closed container in a cool, dry place.

**O. Triethyl citrate**

**Description:** Triethyl citrate is a clear, viscous, odorless and practically colorless, hygroscopic liquid.

**Chemical Name:** 2-Hydroxy-1,2,3-propanetricarboxylic acid, triethyl ester

**Empirical Formula:** $C_{12}H_{20}O_7$

**Molecular Weight:** 276.29

**Functional Category:** Plasticizer.

**Solubility:** It is miscible with ethanol, acetone and iso propyl alcohol.

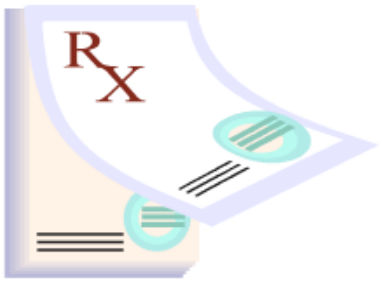
**Applications in Pharmaceutical Formulation or Technology:**

It is used to plasticize polymers in formulated pharmaceutical coatings. The coating applications include capsules, tablets, beads, and granules for taste masking, immediate release, sustained-release and enteric formulations.

**References**

[1] R.C. Rowe, P.J. Sheskey, S.C. Owen, A.P. Association, Handbook of Pharmaceutical Excipients, Pharmaceutical Press, 2006.
[2] A. kasei, Celphere, in, pp. Basic Information on Celphere.
[3] PROSOLV® SMCC, in, JRS Pharma, 2016.

# Appendix-II



**Patent Application**

- **Piyush K. Mundada**, Krutika K. Sawant, Veenu P. Mundada, 'Oral Compositions and Processes for Preparing Different Dosage Forms Comprising of Controlled Release Multi Unit Particulate System' Application No. 1625/MUM/2014., Date of filing of application: 12/05/2014, Publication Date : 27/11/2015, Journal No: 48/2015.

**Publications**

- **Piyush K. Mundada**, Krutika K. Sawant, Veenu P. Mundada. 'Formulation and Optimization of Controlled Release Powder for Reconstitution for Metoprolol Succinate Multi Unit Particulate Formulation using Risk Based QbD Approach'. Manuscript under review in Drug Development and Industrial Pharmacy. [Manuscript ID: LDDI-2016-0652]

- Krutika K. Sawant, **Piyush Mundada**, Dhaval Sodani. 'Physicochemical Characterization And Clinical Evaluation of a Microemulsion System for Topical Delivery of Tazarotene in Psoriasis'. Micro and Nanosystems, 7(2): 98-107, 2015.

- Kiran Ramanlal Chaudhari, Mukesh Ukawala, Arehalli S. Manjappa, Abhinesh Kumar, **Piyush Kishor Mundada**, Anil Kumar Mishra, Rashi Mathur, Jukka Monkkonen and Rayasa S. Ramchandra Murthy. 'Opsonization, Biodistribution, Cellular Uptake and Apoptosis Study of PEGylated PBCA Nanoparticle as Potential Drug Delivery Carrier'. Pharm Res. 2012 Jan;29(1):53-68.

- Parikh K., **Mundada P.** and Sawant K. 'Development of New, Rapid and Validated UV-Spectrophotometric Method for the Estimation of Felbamate in Bulk and Tablets'. Published in Indian Drugs 53 (03) March 2016.

- Krutika Sawant, Mitali Patel, Jiten Patel, **Piyush Mundada. '**Formulation, Optimization, Characterization and in vivo anti-ulcer activity of Esomeprazole magnesium trihydrate gastroresistant microspheres'. Vol. 9, Issue 1, International Journal of Pharmacy and Pharmaceutical Sciences.

- Parikh Kinjal, **Mundada Piyush**, Sawant Krutika. 'Optimization of polymer level by D–optimal design in controlled release felbamate tablet: in-vivo consideration'. Measurement Journal. [Manuscript ID MEAS-D-16-00076]. Manuscript under review.

- Chintan Parmar, Kinjal Parikh, **Piyush Mundada**, Dhaval Bhavsar, Krutika Sawant.' Formulation and optimization of enteric coated mesalamine tablet: In vitro / In vivo investigation and roentogenographic study' Manuscript under review in Drug Development and Industrial Pharmacy. [Manuscript ID: LDDI-2016-0638]

**Poster Presentations**

- **Piyush K. Mundada**, Veenu P. Mundada, Krutika K. Sawant. '*Development and Optimization of Controlled Release Multi Unit Particulate Systems (MUPS) of Antihypertensive Drug by QbD Approach*' presented poster in International Conference on Advances in Formulation Development: Challenges and Applications, organised by Faculty of Pharmacy, Parul University, held on March 4-5, 2016.

- Mundada Veenu, **Mundada Piyush**, Patel Mitali, Dr. Sawant Krutika. '*Regulatory and Statutory Hurdles in Development, Approval and Marketing of Generic Drug Product'* presented poster in 3rd Nirma Institute of Pharmacy International Conference on Global Challenges in Drug Discovery, Development and Regulatory Affairs, held on January 21-23, 2016.

- Parikh Kinjal, **Mundada Piyush**, Sawant Krutika. '*Design and Optimaization of Controlled Release Felbamate Tablets Containing HPMC by D-optimal Mixture Design & in vitro - in vivo investigations'* presented poster in 3rd Nirma Institute of Pharmacy International Conference on Global Challenges in Drug Discovery, Development and Regulatory Affairs, held on January 21-23, 2016.

- Sawant Krutika, Patel Jiten, Patel Mitali, **Mundada Piyush**. '*Formulation, optimization, characterization and in vivo anti-ulcer evaluation of Esomeprazole magnesium trihydrate gastroresistant microspheres'* presented poster in 3rd Nirma Institute of Pharmacy International Conference on Global Challenges in Drug Discovery, Development and Regulatory Affairs, held on January 21-23, 2016.