4.1 Drug profile (Tazarotene)

![Figure 4.1: Structure of Tazarotene](image)

**IUPAC name**

Ethyl 6-[2-(4,4-dimethyl-3,4-dihydro-2H-1-benzo thiopyran-6-yl)ethynyl]pyridine-3-carboxylate

**Formula:** C_{21}H_{21}NO_{2}S

**Mol. mass:** 351.463 g/mol

Tazarotene is a chemical entity which is similar to vitamin A. It helps to renew the skin itself more quickly and which improves the appearance and texture of skin. The tazarotene cream reduces the fine wrinkles which appear due to ageing process on the face, cures mottled light and dark patches on facial skin and benign facial freckles (non-cancerous freckles) in adults and adolescents whose age is above 17 years. The Fabior and Tazorac brands of tazarotene topical are used to treat acne vulgaris in adults and adolescents who are above 12 years. Tazorac is also treats acne (raised, silvery flaking of the skin) in adults.

**Classification of retinoids:-**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>First (non-aromatic retinoids)</td>
<td>Tretinoin (all trans retinoic acid)</td>
</tr>
<tr>
<td>Second (mono-aromatic retinoids)</td>
<td>Etretinate, Acitretin</td>
</tr>
<tr>
<td>Third (mono-aromatic retinoids)</td>
<td>Adapalene, Tazarotene, Bexarotene</td>
</tr>
<tr>
<td>New Retinoid</td>
<td>Seletinoid G</td>
</tr>
</tbody>
</table>
Pharmacodynamics
Tazarotene is a prodrug and a member of the acetylenic class of retinoids. Following topical application, tazarotene undergoes esterase hydrolysis to form its active metabolite, tazarotenic acid. When treating acne tazarotene may be taken in conjunction with an oral antibiotic. Tazarotene has been shown in peer-reviewed double blinded studies to reduce: mottling and hyperpigmentation, shallowness, fine wrinkling and coarse wrinkling in sun damaged skin. Histological studies have shown that long term (greater than 1 year) use of Tazarotene is associated with a significant reduction in atypical melanocytes and keratocytes - cells considered to be precursors of skin cancer. Some studies have shown long term use of Tazarotene to be associated with increased collagen production and better organization of skin collagen bundles.

Mechanism of action
The exact method of tazarotene action is not known, studies have shown that the active form of the drug (tazarotenic acid) binds to all three members of the retinoic acid receptor (RAR) family: RARa, RARb, and RARg, but shows relative selectivity for RARb, and RARg and may modify gene expression. It also has affinity for RXR receptors. In eukaryotic cell, retinoids are transferred to nucleus by CRABP (Cellular Retinoic Acid Binding Protein) predominating in skin. The direct action of retinoid is mediated by RAR (Retinoic acid receptor) and retinoid X receptor.RAR and RXR are member of superfamily of nuclear hormone receptor and having alpha gamma beta subtypes and number of isoforms.

In Tazarotene its active metabolite tazarotenic acid binds selectively to the RAR beta and gamma this leads to formation of homo or hetero dimer receptor complex which in turn bind to specific DNA. This promote gene region called as retinoid rexponse elements (RRE).

Pharmacokinetic
Absorption
Absorption of tazarotene occurs due to its rapid metabolism in the skin to the active metabolite, tazarotenic acid, which can be systemically absorbed and further metabolized.

Distribution
The active form of the drug, tazarotenic acid, is highly bound to plasma proteins (>99%).
Metabolism
Undergo esterase hydrolysis in skin to form its active metabolite, tazarotenic acid. Tazarotenic acid is further metabolized in skin and, after systemic absorption, hepatically metabolized to sulfoxides, sulfones, and other polar products for elimination.

Elimination
Tazarotene and tazarotenic acid are metabolized to sulfoxides, sulfones and other polar metabolites which are eliminated through urinary and fecal pathways.

Side Effects
- Severe irritation on the part of the skin (burning, stinging, itching) after its application;
- Severe redness and discomfort; or
- Swelling, warmth and other signs of skin infection.

Less serious side effects of tazarotene topical may include:
- Mild burning, stinging, or itching;
- Mild pain, redness, or irritation; or
- Skin dryness or peeling.

Contraindications: Pregnancy, lactation, eczema, Sun burnt conditions, Hypersensitivity.

Drug Interactions: Drying of skin is increased with continuous use of this type of medications and cosmetics that have irritant or strong drying effect. Increased risk of photosensitivity with drugs known to be photosensitizes.

Uses
- The therapeutic effect of tazarotene for treating acne may be due to its antihyperproliferative, normalization and differentiation, and anti-inflammatory effects. The cellular mechanisms and inflammatory cascades that might correlate with acne pathogenesis and are modulated by topical tazarotene include:
  - Expressions are reduced due to hyperproliferative keratins K6 and K16, which are increased during comedogenesis.
  - Suppression and activation of the activator protein 1, which results in reduced expression of several matrix metalloproteinase’s from keratinocyte, which have been shown to be increased in acne vulgaris.
Decreased expression of Toll-like receptor (TLR) 2 and decrease in ligand binding with *P. acnes*, which results in inhibition of the TLR-2-induced innate response that triggers inflammation in acne

- Increased epidermal turnover, with reduction in post inflammatory hyperpigmentation
- Normalization of epidermal cellular differentiation and decreased hyperkeratinization
- Down regulated expression of the epidermal growth factor receptor.

**Analytical techniques of Tazarotene**

1. **Roy, et al., 2013**, developed a stability-indicating RP-HPLC method and validated for the simultaneous determination of phenoxyethanol (PE), methylparaben (MP), propylparaben (PP), mometasone furoate (MF), and tazarotene (TA) in topical pharmaceutical dosage formulation. The desired chromatographic separation was achieved on the Waters X-Bridge™ C18 (50×4.6mm, 3.5μ) column using gradient elution at 256 nm detection wavelength. The optimized mobile phase consisted of 0.1%v/v orthophosphoric acid in water as solvent-A and acetonitrile as solvent-B. The method showed linearity over the range of 5.88–61.76 μg/mL, 0.18–62.36 μg/mL, 0.17–6.26 μg/mL, 0.47–31.22 μg/mL, and 0.44–30.45 μg/mL for PE, MP, PP, MF, and TA, respectively. The recovery for all of the components was in the range of 98–102%. The proposed method was successfully applied for the quantitative determination of PE, MP, PP, MF, and TA in a cream sample.

2. **Jogarami et al.,** developed Simple, accurate, and economical procedures for simultaneous estimation of Tazarotene and Hydroquinone in gel form. The method employs formation and solving of simultaneous equation using 247.2 nm and 289.6 nm as two analytical wavelengths for both drugs in methanol. Tazarotene and Hydroquinone at their respective lmax 247.2 nm and 289.6 nm shows linearity in a concentration range of 5-25 μg/ml and 5-25 μg/ml respectively.
4.2 Drug profile (Hydroquinone)

![Figure 4.2: Structure of Hydroquinone](image)

Table 4.2: Description of hydroquinone

<table>
<thead>
<tr>
<th>Name</th>
<th>Hydroquinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUPAC Name</td>
<td>benzene-1,4-diol</td>
</tr>
<tr>
<td>Mol. formula</td>
<td>C₆H₆O₂</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>110 g/mol</td>
</tr>
<tr>
<td>Synonyms</td>
<td>Para-hydroxyphenol; 1,4-dihydroxybenzol; 1,4-dihydroxybenzene; para-dihydroxybenzene; p-benzenediol</td>
</tr>
<tr>
<td>Physical state</td>
<td>Crystalline solid</td>
</tr>
<tr>
<td>Colour</td>
<td>White</td>
</tr>
<tr>
<td>Odor</td>
<td>Odor less</td>
</tr>
<tr>
<td>Melting point</td>
<td>172°C</td>
</tr>
<tr>
<td>Water solubility</td>
<td>Very soluble</td>
</tr>
</tbody>
</table>

Hydroquinone is a chemical entity which is produced industrially in three ways, two of which are dominant. Similar to the cumene process in reaction mechanism, the most widely used route involves the dialkylation of benzene with propene to give 1, 4-diisopropylbenzene. This compound reacts with air to produce the bis-hydroperoxide, whose structure is similar to cumene hydroperoxide and rearranges itself to give acetone and hydroquinone in acid. A second route involves hydroxylation of phenol. The conversion uses hydrogen peroxide and produces a mixture of hydroquinone and catechol.

**Classification of Bleaching or Depigmenting Agents**

*Phenolic compounds*

Hydroquinone

Monobenzyl ether of hydroquinone

4-methoxyphenol
4-isopropylcatechol

*Nonphenolic compounds*

Azelaic acid
Tretinoin
L-ascorbic acid
N-acetylcystein

**Mechanism of action**

Hydroquinine is a hydroxyphenolic chemical entity which inhibits the conversion of dopa to melanin by inhibiting the tyrosinase enzyme. It may also function by interfering with the formation or degradation of melanosomes and by inhibiting the synthesis of DNA and RNA within melanocytes. Its chemical resemblance with certain melanin precursors (tyrosine and dihydroxyphenylalanine) explains its ability to be metabolized in melanocytes as well as its selective action on melaninogenesis. Unlike the monobenzylether of hydroquinone, Hydroquinine is not metabolized to cytotoxic free radicals and, therefore, is not a melanocidal agent. The depigmented effects are limited to the site of application and are usually reversible, although some investigators claim that Hydroquinine can cause permanent or vitiligo-like hypopigmentation, especially in darker skin types. Hydroquinone, or 1,4-dihydroxybenzene, is a Phenolic bleaching compound that is the gold-standard therapy for hypersensitivity. The mechanisms of action of this drug include: (i) reversible inhibition of tyrosinase (the main enzyme involved in the conversion of tyrosine to melanin); and (ii) selective damage to melanosomes and melanocytes.

Therefore, the mechanism of action of topical hydroquinone is through prevention of new melanin production. As skin cells mature, the melanin-containing keratinocyte within the epidermis are shed and new keratinocyte are formed with less pigmented melanosomes. As depicted, the epidermis effectively lightens over time. Hydroquinone is relatively ineffective against dermal hyperpigmentation because it cannot penetrate the dermal–epidermal junction and dermal melanin that is already present has less means of ingress.

**Uses**

- Hydroquinone has many uses which are associated with its action of reducing agent that is soluble in water. It is a main component for most photographic developing films and papers along with the metal compound; it reduces silver halides to elemental silver.
• There are various other uses associated with its reducing power. As a polymerization inhibitor, it prevents polymerization of acrylic acid, methyl methacrylate, cyanoacrylate, and other monomers that are susceptible to radical-initiated polymerization. This application exploits the antioxidant properties of hydroquinone. Hydroquinone can undergo mild oxidation to convert the compound to parabenoquinone, \( \text{C}_6\text{H}_4\text{O}_2 \), often called p-quinine or simply quinone. Reduction of quinone reverses this reaction back to hydroquinone. Some biochemical compounds in nature have this sort of hydroquinone or quinone section in their structures, such as Coenzyme Q, and can undergo similar redox interconversions. Hydroquinone can lose a H+ from both to form a diphenolate ion. The disodium diphenolate salt of hydroquinone is used as an alternating comonomer unit in the production of the polymer peek. Hydroquinone is an aromatic organic compound, which is a white granular solid chemical, synthesized from phenol.

• It is well-known for its antioxidant properties and is used in industry, mainly as an inhibitor for polymerization reaction of monomers in petrochemical industry (for process, transport and storage stabilization).

• It is also used as a stabilizer in the formulation of inks, coatings, rubbers and polymers.

• Hydroquinone is also used as a chemical intermediate for synthesis of pharmaceuticals, chemicals and agrochemicals.

Analytical techniques of Hydroquinone

1. Khoshneviszadeh et al. (2015) developed and validated UV spectrophotometric determination and validation of hydroquinone in liposome. The validation parameters such as linearity, accuracy, precision, specificity, limit of detection (LOD) and limit of quantitation (LOQ) were determined. The calibration curve was linear in 1-50 \( \mu \text{g/mL} \) range of hydroquinone analyte with a regression coefficient of 0.9998. The relative standard deviation values of inter and intra-day precisions were <2%. LOD and LOQ were 0.24 and 0.72 \( \mu \text{g/mL} \) respectively.

2. Lopez Garcia et al., 2005 Estimated high performance liquid chromatographic (HPLC) and a ultraviolet derivative spectrophotometric (UVDS) methods and validated for the quantitative determination of hydroquinone (HQ) in gels and creams containing this compound as a unique active principle. Validation parameters such as linearity, precision, accuracy, specificity, limit of detection (LOD) and limit of
quantitation (LOQ) were determined. HPLC was carried out by reversed phase technique on a RP-18 column with a mobile phase composed of methanol and water (20:80, v/v). The linearity in the range of 6.0–30.0 μg/mL presents a correlation coefficient (r) of 0.9999, calculated by least square method. The LOD and LOQ were 0.14 and 0.46 μg/mL, respectively. Statistical analysis by t- and F-tests, showed no significant difference at 95% confidence level between the two proposed methods.

4.3 Excipients Profile

4.3.1 Cholesterol

Description: Cholesterol occurs as white or faintly yellow, almost odorless, pearly leaflets, needles, powder, or granules. On prolonged exposure to light and air, cholesterol acquires a yellow to tan color (Rowe et al, 2009)

Nonproprietary names
BP : Cholesterol,  
JP : Cholesterol,  
PhEur : Cholesterol  
USP-NF : Cholesterol

Synonyms : Cholesterin; cholesterolum.

Chemical Name and CAS Registry Number : Cholest-5-en-3b-ol [57-88-5]

Empirical Formula : C27H46O

Molecular Weight : 386.67

Functional Category : emollient; emulsifying agent

Structural Formula

![Figure 4.3: Structure of cholesterol]
Applications in pharmaceutical formulation or technology

Cholesterol is used in cosmetics and topical pharmaceutical formulations at concentrations of 0.3–5.0% w/w as an emulsifying agent. It imparts water-absorbing power to an ointment and has emollient activity. Cholesterol also has a physiological role. It is the major sterol of the higher animals, and it is found in all body tissues, especially in the brain and spinal cord. It is also the main constituent of gallstones.

Typical properties

Boiling point : 360°C (some decomposition)
Density : 1.052 g/cm³ for anhydrous form.
Dielectric constant : D₂₀ = 5.41
Melting point : 147–150°C

Stability and storage conditions

Cholesterol is stable and should be stored in a well-closed container, protected from light.

Incompatibilities

Cholesterol is precipitated by digitonin.

Method of manufacture

The commercial material is normally obtained from the spinal cord of cattle by extraction with petroleum ethers, but it may also be obtained from wool fat. Purification is normally accomplished by synthetic means. Cholesterol produced from animal organs will always contain cholesterol and other saturated sterols.

Safety

Cholesterol is generally regarded as an essentially nontoxic and nonirritant material at the levels employed as an excipients. It has, however, exhibited experimental teratogenic and reproductive effects, and mutation data have been reported. Cholesterol is often derived from animal sources and this must be done in accordance with the regulations for human consumption. The risk of bovine spongiform encephalopathy (BSE) contamination has caused some concern over the use of animal derived cholesterol in pharmaceutical products. However, synthetic methods of cholesterol manufacture have been developed.
Handling precautions
Observe normal precautions appropriate to the circumstances and quantity of material handled. Rubber or plastic gloves, eye protection, and a respirator are recommended. May be harmful following inhalation or ingestion of large quantities or over prolonged periods of time, owing to the possible involvement of cholesterol in atherosclerosis and gallstones. May be irritant to the eyes. When heated to decomposition, cholesterol emits acrid smoke and irritating fumes.

Regulatory status
Included in the FDA Inactive Ingredients Database (injections; ophthalmic, topical, and vaginal preparations). Included in nonparenteral medicines licensed in the UK. Included in the Canadian List of acceptable non-medicinal ingredients.

Related substances
Lanolin; lanolin alcohols; lanolin hydrous

Comments
A novel cholesterol-based cationic lipid has been developed that promotes DNA transfer in cells. Cholesterol monohydrate becomes anhydrous at 70–80°C.

4.3.2 Carbopol
Description: Carbomers are white-colored, ‘fluffy’, acidic, hygroscopic powders with a characteristic slight odor. A granular carbomer is also available (Carbopol 71G).

Nonproprietary names
BP : Carbomers
PhEur : Carbomers
USP-NF : Carbomer
Synonyms : Carbopol; carboxy polymethylene; polya crylic acid; carboxyvinyl polymer; Pemulen; Tego Carbomer.

Chemical Name : Carbomer

Empirical Formula and Molecular Weight: Carbomers are synthetic high-molecular-weight polymers of acrylic acid that are crosslinked with either allyl sucrose or allyl ethers of pentaerythritol. They contain between 52% and 68% of carboxylic acid (COOH) groups calculated on the dry basis. The BP 2009 and PhEur 6.4 have a single monograph describing carbomer; the USP32–NF27 contains several monographs describing individual carbomer.
grades that vary in aqueous viscosity, polymer type, and polymerization solvent. The molecular weight of carbomer is theoretically estimated at $7 \times 10^5$ to $4 \times 10^9$. In an effort to measure the molecular weight between crosslinks, MC, researchers have extended the network theory of elasticity to swollen gels and have utilized the inverse relationship between the elastic modulus and MC. Estimated MC values of 237 600 g/mol for Carbopol 941 and of 104 400 g/mol for Carbopol 940 have been reported.

**Structural Formula**

![Figure 4.4: Structure of Carbopol](image)

**Functional category:** Bioadhesive material; controlled-release agent; emulsifying agent; emulsion stabilizer; rheology modifier; stabilizing agent; suspending agent; tablet binder.

**Applications in pharmaceutical formulation or technology:** Carbomers are used in liquid or semisolid pharmaceutical formulations as rheology modifiers. Formulations include creams, gels, lotions and ointments for use in ophthalmic, rectal, topical and vaginal preparations. Carbomer grades with residual benzene content greater than 2 ppm do not meet the specifications of the PhEur 6.4 monograph. However, carbomer having low residuals of other solvents than the ICH-defined ‘Class I OVI solvents’ may be used in Europe. Carbomer having low residuals of ethyl acetate, such as Carbopol 971P NF or Carbopol 974P NF may be used in oral preparations, in suspensions, capsules or tablets. In tablet formulations, Carbomers are used as controlled release agents and/or as binders. In contrast to linear polymers, higher viscosity does not result in slower drug release with carbomers. Lightly cross linked carbomers (lower viscosity) are generally more efficient in controlling drug release than highly crosslinked carbomers (higher viscosity). In wet granulation processes, water, solvents or their mixtures can be used as the granulating fluid. The tackiness of the wet mass may be reduced by including talc in the formulation or by adding certain cationic species to the granulating fluid. However, the presence of cationic salts may accelerate drug release rates and reduce bioadhesive properties. Carbomer polymers have also been
investigated in the preparation of sustained-release matrix beads, as enzyme inhibitors of intestinal proteases in peptide-containing dosage forms, as a bioadhesive for a cervical patch and for intranasally administered microspheres, in magnetic granules for site-specific drug delivery to the esophagus, and in oral mucoadhesive controlled drug delivery systems. Carbomers copolymers are also employed as emulsifying agents in the preparation of oil-in-water emulsions for external administration. Carbomer 951 has been investigated as a viscosity-increasing aid in the preparation of multiple emulsion microspheres. Carbomers are also used in cosmetics. Therapeutically, carbomer formulations have proved efficacious in improving symptoms of moderate-to-severe dry eye syndrome.

**Typical properties**

Density (bulk) 0.2 g/cm³ (powder); 0.4 g/cm³ (granular).
Density (tapped) 0.3 g/cm³ (powder); 0.4 g/cm³ (granular).
Dissociation constant pKa = 6.0 ± 0.5
Glass transition temperature 100–1058°C
Melting point Decomposition occurs within 30 minutes at 2608°C.
Moisture content typical water content is up to 2% w/w.

**Stability and storage conditions:** Carbomers are stable, hygroscopic materials that may be heated at temperatures below 1048°C for up to 2 hours 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 268°C. Dry powder forms of carbomer do not support the growth of molds and fungi. In contrast, microorganisms grow well in unpreserved aqueous dispersions, and therefore an antimicrobial preservative such as 0.1% w/v chlorocresol, 0.18% w/v methylparaben–0.02% w/v propylparaben, or 0.1% w/v thimerosal should be added. The addition of certain antimicrobials, such as benzalkonium chloride or sodium benzoate, in high concentrations (0.1% w/v) can cause cloudiness and a reduction in viscosity of carbomer dispersions.

**Incompatibilities:** Carbomers are discolored by resorcinol and are incompatible with phenol, cationic polymers, strong acids, and high levels of electrolytes. Certain antimicrobial adjuvants should also be avoided or used at low levels. Trace levels of iron and other transition metals can catalytically degrade carbomer dispersions.

**Method of manufacture:** Carbomers are synthetic, high-molecular-weight, crosslinked polymers of acrylic acid. These acrylic acid polymers are crosslinked with allyl sucrose or
allyl pentaerythritol. The polymerization solvent used previously was benzene; however, some of the newer commercially available grades of carbomer are manufactured using either ethyl acetate or a cyclohexane–ethyl acetate cosolvent mixture. The Carbopol ETD and Carbopol Ultrez polymers are produced in the cosolvent mixture with a proprietary polymerization aid.

**Safety:** Carbomers are used extensively in nonparenteral products, particularly topical liquid and semisolid preparations. Grades polymerized in ethyl acetate may also be used in oral formulations. There is no evidence of systemic absorption of carbomer polymers following oral administration. Acute oral toxicity studies in animals indicate that carbomer 934P has a low oral toxicity, with doses up to 8 g/kg being administered to dogs without fatalities occurring. Carbomers are generally regarded as essentially nontoxic and nonirritant materials; there is no evidence in humans of hypersensitivity reactions to carbomers used topically (Sheskey et al, 2009).

### 4.3.3 Lecithin

**Description:** Lecithin’s vary greatly in their physical form, from viscous semi liquids to powders, depending upon the free fatty acid content. They may also vary in color from brown to light yellow, depending upon whether they are bleached or unbleached or on the degree of purity. When they are exposed to air, rapid oxidation occurs, also resulting in a dark yellow or brown color. Lecithin’s have practically no odor. Those derived from vegetable sources have a bland or nutlike taste, similar to that of soybean oil (Sheskey et al, 2009).

**Nonproprietary names**

USP-NF: Lecithin

**Synonyms:** E322; egg lecithin; LSC 5050; LSC 6040; mixed soybean phosphatides; ovolecithin; Phosal 53 MCT; Phospholipon 100 H; ProKote LSC; soybean lecithin; soybean phospholipids; Sternpur; vegetable lecithin.

**Chemical name:** Lecithin

**Empirical formula and molecular weight:** The USP32–NF27 describes lecithin as a complex mixture of acetone-insoluble phosphatides that consists chiefly of phosphatidylcholine, phosphatidylethanolamine, phosphatidylerine, and phosphatidylinositol, combined with various amounts of other substances such as
triglycerides, fatty acids, and carbohydrates as separated from a crude vegetable oil source. The composition of lecithin (and hence also its physical properties) varies enormously depending upon the source of the lecithin and the degree of purification. Egg lecithin, for example, contains 69% phosphatidylcholine and 24% phosphatidylethanolamine, while soybean lecithin contains 21% phosphatidylcholine, 22% phosphatidylethanolamine, and 19% phosphatidylinositol, along with other components.

**Structural formula**

![Figure 4.5: Structure of lecithin](image)

**Functional category:** Emollient; emulsifying agent; solubilizing agent.

**Applications in pharmaceutical formulation or technology:** Lecithin’s are used in a wide variety of pharmaceutical applications. They are also used in cosmetics and food products. Lecithin’s are mainly used in pharmaceutical products as dispersing, emulsifying, and stabilizing agents, and are included in intramuscular and intravenous injections, parenteral nutrition formulations, and topical products such as creams and ointments. Lecithins are also used in suppository bases, to reduce the brittleness of suppositories, and have been investigated for their absorption-enhancing properties in an intranasal insulin formulation. Lecithin’s are also commonly used as a component of enteral and parenteral nutrition formulations.

There is evidence that phosphatidylcholine (a major component of lecithin) is important as a nutritional supplement to fetal and infant development. Furthermore, choline is a required component of FDA-approved infant formulas. Other studies have indicated that lecithin can protect against alcohol cirrhosis of the liver, lower serum cholesterol levels, and improve mental and physical performance. Liposomes in which lecithin is included as a component of the bilayers have been used to encapsulate drug substances; their potential as novel delivery systems has been investigated. This application generally requires purified lecithins combined in specific proportions.
Drugs Profile

Therapeutically, lecithin and derivatives have been used as a pulmonary surfactant in the treatment of neonatal respiratory distress syndrome.

**Stability and storage conditions:** Lecithin’s decompose at extreme pH. They are also hygroscopic and subject to microbial degradation. When heated, lecithins oxidize, darken, and decompose. Temperatures of 160–180°C will cause degradation within 24 hours. Fluid or waxy lecithin grades should be stored at room temperature or above; temperatures below 108°C may cause separation. All lecithin grades should be stored in well-closed containers protected from light and oxidation. Purified solid lecithin should be stored in tightly closed containers at subfreezing temperatures.

**Incompatibilities:** Incompatible with esterases owing to hydrolysis.

**Safety:** Lecithin is a component of cell membranes and is therefore consumed as a normal part of the diet. Although excessive consumption may be harmful, it is highly biocompatible and oral doses of up to 80 g daily have been used therapeutically in the treatment of tardive dyskinesia. When used in topical formulations, lecithin is generally regarded as a nonirritant and nonsensitizing material.(2) The Cosmetic Ingredients Review Expert Panel (CIR) has reviewed lecithin and issued a tentative report revising the safe concentration of the material from 1.95% to 15.0% in rinse-off and leave-in products. They note, however, that there are insufficient data to rule on products that are likely to be inhaled.

**Handling precautions:** Observe normal precautions appropriate to the circumstances and quantity of material handled. Lecithins may be irritant to the eyes; eye protection and gloves are recommended.

4.3.4 **Soya phosphotidyl choline**

**Synonyms**

1, 2-Diacyl-\(sn\)-glycero-3-phosphocholine; 3-\(sn\)-osphatidylycholine; L-\(\alpha\)-

**Biological source:** Soyabean

**Molecular weight:** 776 g/mol

**Description:** yellow to very dark yellow, soft granular powder. Typical lots of pure soybean phosphatidylcholine have fatty acid contents of approximately 13% C16:0 (Palmitic), 4% C18:0 (Stearic), 10% C18:1(oleic), 64% C18:2 (linoleic), and 6% 18:3 (linolenic) with other fatty acids being minor contributors.

**Melting point:** 188 °C
Storage temperature: 2 - 8 °C
Assay: 14 - 23% based on choline basis

Structure:

![Structure of soyaphosphatidyl choline](image)

Phosphatidylcholine is the major membrane phospholipid in eukaryotic cells. In addition to being the major structural component of cellular membranes, phosphatidylcholine serves as a reservoir for several lipid messengers. It is the source of the bioactive lipids lysophosphatidylcholine, phosphatidic acid, diacylglycerol, lysophosphatidylcholine, platelet activating factor, and arachidonic acid (Kent and Carman, 1999). An understanding of the control and regulation of the several metabolic pathways involved in the formation of these bioactive lipids is an ongoing science. Apart from that, it is used as a main component in the preparation of Liposomes, applicable for sustained or site specific delivery.

4.3.5 Polyethylene glycol

**Synonyms**: polyethylene oxide (PEO) or polyoxyethylene (POE)

**Nomenclature**: Poly (ethylene oxide) or poly (oxyethylene)

**Chemical formula**: \( C_{2n}H_{4n+2}O_{n+1} \)

**Molecular Weight**: \( 18.02 + 44.05n \text{ g/mol} \)

**Chemical structure**:

![Structure of Polyethylene glycol](image)

**Solubility**: PEG is soluble in water, methanol, ethanol, acetonitrile, benzene, and dichloromethane, and is insoluble in diethyl ether and hexane.
**Stability:** PEG are chemically stable in air and in solution, although grades with a molecular weight less than 2000 are hygroscopic (Grassie and Scott, 1985).

**Application:** The chemistry and biological applications of polyethylene glycol (or "PEG") have been the subject of intense study both in academics and in industry.

**Storage:** Propylene Glycols should be stored at ambient temperatures in closed containers and away from sunlight and other sources of UV light.

**Safety:** it is generally regarded as relatively nontoxic and nonirritant materials, although it has occasionally been reported to cause hypersensitivity reactions including urticaria and allergic response.

**Side effect:**
- Full or bloated feeling
- pain in the upper stomach
- pressure in the stomach
- stomach pain
- swelling of abdominal or stomach area
- vomiting

**Uses**
- PEG is the basis of a number of laxatives. Whole bowel irrigation with polyethylene glycol and added electrolytes is used for bowel preparation before surgery or colonoscopy.
- PEG is also used as an excipients in many pharmaceutical products.
- When attached to various protein medications, polyethylene glycol allows a slowed clearance of the carried protein from the blood.
- PEG is commonly used as a precipitant for plasmid DNA isolation and protein crystallization. X-ray diffraction of protein crystals can reveal the atomic structure of the proteins.
- PEG is used to fuse two different types of cells, most often B-cells and myelomas in order to create hybridomas.
- Polyethylene glycol has a low toxicity and is used in a variety of products. The polymer is used as a lubricating coating for various surfaces in aqueous and non-aqueous environments.
4.3.6 Methyl paraben

- **IUPAC name:** Methyl 4-hydroxybenzoate
- **Formula:** $\text{C}_8\text{H}_8\text{O}_3$
- **Molecular weight:** 152.15 g·mol$^{-1}$

**Description:** Methylparaben, also methyl paraben, one of the paraben, is a preservative with the chemical formula $\text{CH}_3(\text{C}_6\text{H}_4(\text{OH})\text{COO}).$ It is the methylester of $p$-hydroxybenzoic acid (Sheskey et al., 2009).

- **Structure**

![Structure of Methyl Paraben](image)

**Figure 4.8: Structure of Methyl Paraben**

- **Boiling point:** 270-280°C.
- **Density:** 1.38 g/cm$^3$ at 20°C
- **Melting point:** 125-128°C

**Solubility:** Soluble in water (2.5 g/l) at 25°C, benzene (slightly soluble), carbon tetrachloride (slightly soluble), ethanol, ether, acetone, DMSO, methanol, warm oil (25 g/l), and warm glycerol (1 g/70 ml).

**Uses:** Methylparaben is an anti-fungal agent often used in a variety of cosmetics and personal-care products. It is also used as a food preservative and has the E number E218.

Methylparaben is commonly used as a fungicide in *Drosophila* food media. To *Drosophila*, Methylparaben is toxic at higher concentrations, has an estrogenic effect, and slows the growth rate in the larval and pupal stages at lower concentrations.

**Safety:** There is controversy about whether Methylparaben or propylparaben are harmful at concentrations typically used in body care or cosmetics. Methylparaben and propylparaben are considered generally recognized as safe (GRAS) for food and cosmetic antibacterial preservation. Methylparaben is readily metabolized by common soil bacteria, making it completely biodegradable.
Methylparaben is readily absorbed from the gastrointestinal tract or through the skin. It is hydrolyzed to \( p \)-hydroxybenzoic acid and rapidly excreted in urine without accumulating in the body. Acute toxicity studies have shown that Methylparaben is practically non-toxic by both oral and parenteral administration in animals. In a population with normal skin, Methylparaben is practically non-irritating and non-sensitizing; however, allergic reactions to ingested paraben have been reported.

Studies indicate that Methylparaben applied on the skin may react with UVB, leading to increased skin aging and DNA damage.

### 4.3.7 Propyl paraben

- **IUPAC name:** Propyl \( 4 \)-hydroxybenzoate
- **Chemical formula:** \( C_{10}H_{12}O_3 \)
- **Molecular weight:** 180.2 g/mol
- **Description:** Propylparaben, the \( n \)-Propyl ester of \( p \)-hydroxybenzoic acid, occurs as a natural substance found in many plants and some insects, although it is manufactured synthetically for use in cosmetics, pharmaceuticals and foods. It is a preservative typically found in many water-based cosmetics, such as creams, lotions, shampoos and bath products. As a food additive, it has the E number E216. Propyl Paraben is an odorless, extra fine, white powder that is non-hygroscopic and generally recognized as safe (GRAS) for use as a preservative in foods.

- **Structure**

![Figure 4.9: Structure of Propyl Paraben](image)

- **Boiling point:** 133°C
- **Density:** 1.0630 g/cm\(^3\)
- **Melting point:** 96 – 99°C
**Solubility:** Soluble in Propylene glycol, ethanol, ether, acetone, methanol, and DMSO. Very slightly soluble in Glycerin, and Insoluble in Water.

**Stability:** Stable. Incompatible with strong oxidizing agents, strong bases.

**Uses:** Propyl paraben is an antimicrobial chemical used as a preservative in packaged foods, pharmaceuticals, cosmetics, and personal care products (Sheskey *et al*, 2009).