2.1. Drug Profile: Silymarin

2.1.1. Source

Silymarin (Silybum marianum) is extracted from the seeds of the milk thistle plant, which is a member of the Asteraceae (Kaen et al 2005) (Figure 8). Milk thistle is an annual or biennial herb that grows from 1.5 to 3.0 m tall, has large prickly-edged leaves covered with undulating white patches, and stems containing a milky juice (Dixit et al 2007). Silymarin is often called milk thistle extract because its seeds contain about 70 percent of the phytonutrient according to the “Encyclopedia of Natural Medicine." Other parts of the milk thistle plant, such as the sprouts and stems, also contain silymarin, but the seeds are the most concentrated form. Milk thistle is extracted for the flavonolignans, silychristin, silydianin, silybinin A, silybinin B, isosilybinin A and isosilybinin B, which are collectively known as the silymarin complex (Lee and Liu 2003). These unique phytochemicals from the milk thistle have been the subject of decades of research into their beneficial properties.

Figure 8: Milk thistle plant with flower

2.1.2. History and origin

Milk thistle is indigenous to countries in Mediterranean region, where it is taken as a medicinal plant. The milk thistle plant originates from the Mediterranean but is now cultivated in most parts of the world with moderate temperatures, including Canada, Europe, and the United States. In North America, milk thistle is often regarded as a weed and a target of pesticides. It may poison cattle and other livestock that eat large amounts of whole plants.
Silymarin is derived from ancient European medicinal practices (Schadewaldt 1969). Silymarin first appears as Silubon in book four of the five volume treatise on medicine known De Materia Medica (On Medical Matters). While silymarin is considered part of Traditional Chinese Medicine (Efferth et al 2007). During the last years the use of milk thistle is tested by multiple scientific studies, conducted mainly in Germany. The German Health Authorities (equivalent to the U.S. Food and Drug Administration) founded a special Commission E, which is supposed to develop the rules (dosages, indications, and contraindications) of milk thistle preparations usage to promote the best health benefits. Nowadays the plant becomes more familiar to the American consumers, too, gaining their confidence and trust in its power and health benefits. Since milk thistle is easy to grow, it is already cultivated in many states throughout the country (Mendoza et al 2014).

2.1.3. Chemical Structure

The common point of all structural isomers was a flavonolignan skeleton (Figure 9). The main constituents of silymarin are silybin A, silybin B, isosilybin A, isosilybin B, silychristin A, silychristin B and silydianin (Figure 10). A number of other chemically related compounds have been found in the milk thistle fruit including dehydro silybin, desoxysilychristin, desoxysilydianin, silandrin, silybinome, and neo silymarin (Kvasnicka et al 2003). The common feature of these compounds is a flavonolignan skeleton (C_{25}H_{22}O_{10}). Specially, flavonolignan nucleus consists dihydroflavanol, taxifolin linked to coniferyl alcohol moiety through an oxeran ring. The oxeran ring is responsible for the biological activity of silymarin, and opening of this ring results loss of activity (White et al 2007).

The main chemical difference between silymarin and other flavonoids is that its isomers are substituted by a coniferyl alcohol group. Of the three isomers that constitute silymarin, silibinin is the most active.
Figure 9: Chemical and three dimensional structure of silymarin

Figure 10: Chemical structures of the silymarin flavonolignans from milk thistle
2.1.4. Chemical Formula

Molecular formula: C_{25}H_{22}O_{10}

2.1.5. IUPAC Name

(2S)-3,5,7-trihydroxy-2-{(2S,3R)-3-(4-hydroxy-3-methoxyphenyl)-2-(hydroxymethyl)-2,3-dihydro-1,4-benzodioxin-6-yl}-2,3-dihydrochromen-4-one

2.1.6. Molecular weight

Silymarin molecular weight is 482.44

2.1.7. Appearance and Melting point

Yellow colour and melting point is 230-233°C

2.1.8. Solubility

Low water solubility (0.04 mg/mL) of silymarin is reported. Solubility of silymarin in various other solvents like transcutol, ethanol, polysorbate 20, and glyceryl monooleate is 350.1 mg/mL, 225.2 mg/mL, 131.3 mg/mL, and 33.2 mg/mL, respectively (Fenyvesi et al 2011).

Bioavailability is the primary and most active component of the silymarin complex. Orally administered silymarin (silybin) is rapidly absorbed with a t_{max} (2-4 hours) and t_{1/2} (6 hours). Only 20-50 % of oral silymarin is absorbed from the gastrointestinal tract where it undergoes extensive enterohepatic circulation. Therefore, absorption of silymarin from the gastrointestinal tract is low, making bioavailability poor. It was reported that there is 0.73% oral bioavailability of silymarin (standardized as silybin) in rat plasma. In research tissue distribution experiments in mice it has been reported that silybin (50 mg/kg), both in free and conjugated form (e.g., glucuronide and sulfate conjugated forms), was quickly absorbed after oral administration and has a good tissue distribution profile in various tissues examined (Javed and Kohli 2011).

The four major causes of limited silymarin bioavailability are extensive phase II metabolism, low permeability across intestinal epithelial cells, low aqueous solubility, and rapid excretion in bile and urine. These factors necessitate the incorporation of silymarin into a form that can augment its bioavailability (Passerini et al 2012).
2.1.9. Method of Extraction

European Pharmacopoeia recommends a two-step process of silymarin extraction: First, the fruits are defatted for 6 hr, using n-hexane; second, silymarin is extracted with methanol for 5 more hours. Since this method uses large amounts of toxic solvents and forms too much waste, researchers, have focused on alternative methods of plant sample preparation that allow for elimination of the drawbacks of the traditional approach. Reflux technique gave a reasonable silymarin content (968.12 ppm) while in maceration with shaking still better yield was (1419.9 ppm) obtained (Wianowska et al 2015). Content of silymarin was reported to be 722.8 ppm in extract by Soxhlet after pre-treatment of seeds with acids and base. Hot water is gaining attention as an extraction solvent in the recovery of compounds from plant material as it is a green solvent.(Dorota et al 2015). Although subcritical water shows significant promise in replacing organic solvents as an extraction solvent, compound degradation has been observed at elevated extraction temperatures (Ghafor et al 2014) (Abigali et al 2008)

2.1.10. Pharmacological Action

Silymarin has multiple actions as a hepatoprotective agent. The antioxidant property and cell-regenerating functions as a result of increased protein synthesis are considered as most important action.

(i) Antioxidant property: The cytoprotective effects of silymarin are mainly attributable to its antioxidant and free radical scavenging properties. Silymarin can also interact directly with cell membrane components to prevent any abnormalities in the content of lipid fraction responsible for maintaining normal fluidity.

(ii) Stimulation of protein synthesis: Silymarin can enter inside the nucleus and act on RNA polymerase enzymes resulting in increased ribosomal formation. This in turn hastens protein and DNA synthesis.

(iii) Anti-inflammatory actions: The inhibitory effect on 5-lipoxygenase pathway resulting in inhibition of leukotriene synthesis is a pivotal pharmacological property of silymarin.
(iv) Antifibrotic action: Silymarin inhibits NF-B and also retards HSC activation. It also inhibits protein kinases and other kinases involved in signal transduction and may interact with intracellular signalling pathways.

(v) Silibenin (SB), silydianin (SD), and silychristin (SC) are components of silymarin. These compounds can be used to protect the skin from oxidative stress induced by ultraviolet (UV) irradiation and to treat it. To this end, the absorption of silymarin constituents via the skin was examined in research.

(vi) Various tests performed on human skin have shown that constituents of silymarin possess marked anti-inflammatory and anti-carcinogenic properties, if applied before and even after day light exposure.

(vii) Drug and toxin related liver damage: Silymarin has a regulatory action on cellular and mitochondrial membrane permeability in association with an increase in membrane stability against xenobiotic injury. It can prevent the absorption of toxins into the hepatocytes by occupying the binding sites as well as inhibiting many transport proteins at the membrane. These actions along with antiperoxidative property make silymarin a suitable candidate for the treatment of iatrogenic and toxic reactions.

(viii) Silymarin has activity against a broad range of cancer types, and an examination of the literature revealed that silymarin has impressive effects against prostate cancer, colon cancer, ovarian cancer, skin cancer, lung cancer, breast cancer and cervical cancers in preliminary studies. In the cases of prostate and ovarian cancer, human clinical trials are currently underway both in the USA and Europe (Fraschini et al 2002) (Maghrani et al 2004).

2.1.11. Marketed Products

Silymarin in combination is manufactured by 58 companies in different dosage form: tablet, syrup, cream, gel, ointment, liquid and injection. 92 brands of silymarin generics are listed as: Alcohep (Capsule), Aloliv (suspension), Aloliv Cap, Arosi (Tablet), Askaliv (Suspension), Askaliv Suspension, Askaliv Sachet, Askaliv Capsule, Baroliv Oral suspension, Baroliv DPS (Oral drops), Eliv Silymarin (Capsule), Eliv (Syrup), Good Liver Syrup, Hepa Silymarin (Tablet), Hepagreen Plus (Tablet)
Since then, hundreds of studies have been done on silymarin, and it has been approved in the German Commission E Monographs as a supportive treatment for inflammatory liver conditions such as cirrhosis, hepatitis, and fatty infiltration caused by alcohol and other toxins. The medicinal ingredient may comply with the specifications outlined in the pharmacopoeia monographs listed in Table 3 below.

Silymarin is included in the pharmacopoeia of many countries (shown in Table 3) and is often used as supportive therapy in food poisoning due to fungi and in chronic liver disorders, such as steatosis and alcohol-related liver disease.

<table>
<thead>
<tr>
<th>Pharmacopoeia</th>
<th>Monograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>USP</td>
<td>Milk Thistle</td>
</tr>
<tr>
<td></td>
<td>Powdered Milk Thistle</td>
</tr>
<tr>
<td></td>
<td>Powdered Milk Thistle Extract</td>
</tr>
<tr>
<td></td>
<td>Milk Thistle Capsules</td>
</tr>
<tr>
<td></td>
<td>Milk Thistle Tablets</td>
</tr>
<tr>
<td>BP</td>
<td>Milk Thistle Fruit</td>
</tr>
<tr>
<td>Ph. Eur.</td>
<td>Milk Thistle Fruit</td>
</tr>
<tr>
<td></td>
<td>Milk Thistle Dry Extract</td>
</tr>
</tbody>
</table>

2.1.12. Dose

Topical: 6-9 mg per day for topical application (Katiyar et al 1997)
Oral: 140 mg for hepatic disease (Karmi et al 2011)

2.1.13. Stability and Storage

Susceptible to oxidation in air and degrades in light

2.1.14. Pharmacokinetic Profile

The absorption by oral route is low. About 20-40 percent of the administered dose of silymarin is excreted in bile as sulphates and glucuronide conjugates in human beings.
Elimination half-life is approximately 6 h. Silymarin is reported to have a very good safety profile. Both animal and human studies showed that silymarin is non toxic even when given at high doses.

2.1.15. Adverse Effects

Most commonly noted adverse effects were related to gastrointestinal tract like bloating, dyspepsia, nausea, irregular stool and diarrhoea. It also produced pruritus, headache, exanthema, malaise, asthenia, and vertigo in few cases (Saller et al 2001) (Kren et al 2005)

2.1.16. Drug interactions

While silymarin appears to have few side effects, it is not known whether it exerts any drug interaction with interferon, ribavirin, lamivudine, or other conventional treatment for hepatitis B. Silymarin is known to interact with other drugs like Alprazolam, Clopidogrel, Diazepam, Fexofenadine, Lorazepam, Lovastatin, Warfarin.

2.1.17. Contraindications

- Contraindicated in pregnancy
- Contraindicated in lactation
- Contradicted in case of Hypersensitivity (Karimi et al 2011) (Gupta et al 2008)

2.1.18. Procurement

Drug was procured from “Alchem International limited”

Organoleptic Evaluation: Silymarin is yellow in colour and odourless

Assay of Drug: Percentage purity of the drug was found to be within limit (as per certificate of analysis provided by silymarin supplier) Figure 11
### Figure 11: Certificate of Analysis

Below is the certificate of analysis for a particular product. The certificate includes various tests and their results. Here is the tabulated information:

<table>
<thead>
<tr>
<th>Test</th>
<th>Requirement/Limit</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Free-flowing powder</td>
<td>Free-flowing powder</td>
</tr>
<tr>
<td>Colour</td>
<td>Yellowish brown</td>
<td>Yellowish brown</td>
</tr>
<tr>
<td>Identification</td>
<td>UV spectrum of sample should match with working standard spectrum</td>
<td>UV spectrum of sample matched with working standard spectrum</td>
</tr>
<tr>
<td>Total Ash</td>
<td>≤ 0.20%</td>
<td>0.08%</td>
</tr>
<tr>
<td>Loss on Drying</td>
<td>≤ 0.10%</td>
<td>0.06%</td>
</tr>
<tr>
<td>Assay (by UV)</td>
<td>70%</td>
<td>76.70%</td>
</tr>
<tr>
<td>Residual Solvent</td>
<td>≤ 3000 p.p.m.</td>
<td>962 p.p.m.</td>
</tr>
</tbody>
</table>

On the basis of above tests, the material is found to comply with the specified specifications as per Analytical Protocol and Product Specification.

Prepared by: [Signature]

Checked by: [Signature]

Manager Q.C.

Contact: Telephone: 31-123-4567890 Fax: 31-123-4567890, 3239890, 3298981, 3207871, 3201190
E-mail: contact@alchmiinternational.com
2.2. Drug Profile: 5-Fluorouracil

2.2.1. Chemical Name: 5-Fluorouracil

2.2.2. Molecular weight: 130.08

2.2.3. Molecular Formula: $\text{C}_4\text{H}_3\text{FN}_2\text{O}_2$

2.2.4. IUPAC Name: 5-fluoro-1,2,3,4-tetrahydropyrimidine-2,4-dione

2.2.5. Structure

![Chemical structure of Fluorouracil]

Figure 12: Chemical structure of Fluorouracil

2.2.6. Indications and topical use of Fluorouracil

- For actinic or solar keratosis treatment
- For the treatment of superficial basal cell carcinomas, when conventional methods are impractical, such as with multiple lesions.
- Fluorouracil injection is indicated in the palliative management of some types of cancer, including colon, esophageal, gastric, rectum, breast, biliary tract, stomach, head and neck, cervical, pancreas, renal cell, and carcinoid
2.2.7. Overdose

Topical overdose will not cause acute problems. If Fluorouracil cream is ingested, it induce emesis and gastric lavage. Administer symptomatic and supportive care as needed. If it comes in contact with the eye, flush with large amounts of water.

2.2.8. Physical Description

FU is white to near white crystalline powder

2.2.9. Odour

Practically Odorless

2.2.10. Melting Point

Decomposes at 282-283 °C

2.2.11. Solubility

Soluble in methanol water mixture, sparingly soluble in alcohol and propylene glycol

2.2.12. Stability

Stable when exposed to air

2.2.13. Fluorouracil topical cream and Administration

Fluorouracil Cream USP, 0.5% (Microsphere) should be applied once a day to the skin where actinic keratosis lesions appear, using enough to cover the entire area with a thin film.

Fluorouracil Cream USP, 0.5% (Microsphere) should be applied ten minutes after thoroughly washing, rinsing, and drying the entire area.

Fluorouracil Cream USP, 0.5% (Microsphere) may be applied using the fingertips. Immediately after application, the hands should be thoroughly washed.

Fluorouracil Cream USP, 0.5% (Microsphere) should be applied up to 4 weeks as tolerated. Continued treatment up to 4 weeks results in greater lesion reduction.

2.2.14. Therapeutic uses

- Antimetabolite, Antineoplastic and Immunosuppressive agent
- Fluorouracil is used for palliative treatment of carcinoma of the colon, rectum, breast, stomach, and pancreas in patients considered to be incurable by surgery or other means.
- Fluorouracil is used for treatment of bladder carcinoma, prostatic carcinoma, epithelial ovarian carcinoma, cervical carcinoma, endometrial carcinoma, anal
carcinoma, esophageal carcinoma, metastatic tumors of skin carcinoma, and hepato blastoma, and is used by intra-arterial injection for treatment of hepatic tumors and head and neck tumors.

- In combination therapy, in the management of adrenocortical carcinoma, vulvar carcinoma, penile carcinoma and carcinoid tumors (gastrointestinal and neuroendocrine tumors).
- Fluorouracil is used for the treatment of glaucoma during or following trabeculectomy surgery

2.2.15. Mechanism of action

- Fluorouracil showed action by binding to thymidylate synthase and form ternary complex which inhibits the conversion of thymidylate to uracil, so interfering with DNA synthesis.
- Fluorouracil also interferes with RNA processing and protein synthesis.
- Fluorouracil also interferes with cell division for S phase of cell cycle. It inhibits formation of DNA and RNA synthesis. DNA and RNA are essential for cell division and growth, the effect of fluorouracil may be to create a thymine deficiency which provokes unbalanced growth and death of the cell (William et al 1970) (Longley et al 2003).

2.2.16. Adverse effect during topical overdose

Local pain, itching, burning, stinging, crusting, weeping, dermatitis, photosensitivity

2.2.17. Contraindications

- Person who have Dihydropyrimidine Dehydrogenase Deficiency, Shallow Skin Ulcer, and Pregnant and mother who is breast feeding his child
- Person allergic to Pyrimidine analogues (Blasco et al 2008)

2.2.18. Marketed Topical formulations of Fluorouracil

Marketed topical formulation of Fluorouracil is listed as below:
### Table 2: Marketed formulation of Fluorouracil

<table>
<thead>
<tr>
<th>Name</th>
<th>Dosage form</th>
<th>Strength</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolak</td>
<td>Cream</td>
<td>.04 g/g</td>
<td>Hill Dermaceuticals</td>
</tr>
<tr>
<td>Fluoroplex</td>
<td>Cream</td>
<td>10 mg/g</td>
<td>Aqua Pharmaceuticals</td>
</tr>
<tr>
<td>Fluoroplex Cream 1%</td>
<td>Cream</td>
<td>1 %</td>
<td>Allergan Herbert</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Solution</td>
<td>50 mg/mL</td>
<td>Solco healthcare</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Solution</td>
<td>20 mg/mL</td>
<td>Solco healthcare</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Cream</td>
<td>5 mg/g</td>
<td>Mylan Pharmaceuticals</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Cream</td>
<td>5 mg/g</td>
<td>Spear Dermatology Products</td>
</tr>
<tr>
<td>Carac</td>
<td>Cream</td>
<td>5 mg/g</td>
<td>Dermik Laboratories</td>
</tr>
<tr>
<td>Carac</td>
<td>Cream</td>
<td>5 mg/g</td>
<td>Valeant Pharmaceuticals</td>
</tr>
<tr>
<td>Efudex</td>
<td>Cream</td>
<td>2 g/40g</td>
<td>Valeant</td>
</tr>
<tr>
<td>Efudex Cream 5%</td>
<td>Cream</td>
<td>5 %</td>
<td>Valeant Pharmaceuticals</td>
</tr>
</tbody>
</table>

For the preparation of topical delivery system for silymarin, it is required that they are combined with other excipients to form NLC gel for topical application. To be formulated silymarin in to NLC, number of major excipients required such as lipids and surfactants.

### 2.3. Excipient Profile

#### 2.3.1. Glycerol monostearate

**2.3.1.1. Synonym:** Glyceril monostearate, Glycerin monostearate and Monostearin
2.3.1.2. Chemical structure

![Chemical structure of Glycerol monostearate](image)

Figure 13: Chemical structure of Glycerol monostearate

2.3.1.3. Molecular Formula: \( \text{C}_{21}\text{H}_{42}\text{O}_4 \)

2.3.1.4. Molecular weight: 358.56 g·mol\(^{-1}\)

2.3.1.5. Melting point: 58 to 59 °C

2.3.1.6. Appearance: white to yellowish solid

2.3.1.7. Solubility: In water it is Insoluble

2.3.1.8. Iodine value: 2 g \( \text{I}_2/g \)

2.3.1.9. Saponification value: 160-175 mg KOH/g

2.3.1.10. Odour: Light

2.3.1.11 Free fatty acid: 1 %

2.3.1.12. Monoglyceride content: 40 %

2.3.1.13. Storage conditions

This product remains stable for 12 months from date of manufacturing, when it is stored at ambient conditions away from moisture inlet and direct sunlight.

2.3.1.14. Functional category

- Glycerol monostearate is an organic molecule used as an emulsifier

- It is a glycerol ester of stearic acid. This is the ester of glycerol and one molecule of stearic acid and used in the manufacture of cosmetic creams and dermatologic preparations
• It occurs naturally in the body as a product of the breakdown of fats by pancreatic lipase, and is also found in fatty foods

• Glycerol Monostearate is a white powder lipophilic non-ionic surfactant with 40% monoglycerides content. It has effects of emulsification, dispersion, foaming, defoaming, starch anti-aging and fat agglomeration control. It is derived from Kosher certified materials for wider acceptance of use.

2.3.1.15. Regulatory status

• Direct food substances affirmed as generally recognized as safe in listing of specific substances affirmed as GRAS

2.3.2. Oleic acid

2.3.2.1. Synonym: Oleic acid. (9Z)-Octadecenoic acid, (Z)-Octadec-9-enoic acid, cis-9-Octadecenoic acid

2.3.2.2. Chemical structure:

![Chemical structure of Oleic acid](image)

Figure 14: Chemical structure of Oleic acid

2.3.2.3. Molecular Formula: \( C_{18}H_{34}O_2 \)

2.3.2.4. Molecular weight: 282.47 g mol\(^{-1}\)

2.3.2.5. Melting point: 13 to 14 °C
2.3.2.6. Appearance: Oleic acid is a colourless to pale yellow liquid with a mild odour.

2.3.2.7. Solubility: Soluble in ethanol, practically insoluble in water; soluble in chloroform, ether, alcohol, acetone, benzene, chloroform and carbon tetrachloride.

2.3.2.8. Odour: Lard like odour

2.3.2.9. Storage conditions: Keep containers closed and store in cool and dark place. On exposure to air, especially when impure, it oxidizes & acquires yellow to brown colour & rancid odour

2.3.2.10. Functional category

- Oleic acid is used as an excipient as an emulsifying or solubilizing agent in pharmaceuticals
- Oleic acid and its salt is a main component of soap as an emulsifying agent.
- It is also used as an emollient, and also used commercially in the preparation of lotions

2.3.2.11. Regulatory status

In can be safely used as a lubricant, binder, and defoaming agent in accordance with good manufacturing practice.

2.3.3. Miglyol 812

2.3.3.1. Description: Caprylic/capric Triglyceride

2.3.3.2. Molecular Formula: \( C_{11}H_{23}C_{12}NO_3 \)

2.3.3.3. Molecular weight: 278.13182 g/mol

2.3.3.4. Physical state: Liquid

2.3.3.5. Colour: light yellow
2.3.3.6. **Iodine value:** 0.5 mg l/100 mg

2.3.3.7. **Saponification value:** 325-345 mg KOH/g

2.3.3.7. **Solubility:** In hexane, toluene, diethyl ether, ethyl acetate, acetone, isopropanol and ethanol soluble at 20 °C. It is not soluble in water and glycerol

2.3.3.8. **Storage conditions:** Store in tightly closed container and at dry place

2.3.3.9. **Applications:** Widely used in cosmetic and topical dosage form due to its good spreadability on the skin and skin absorption. It have excellent penetration enhancing emollient and skin-smoothing properties.

---

2.3.4. **Compritol 888 ATO**

2.3.4.1. **Synonym:** Glyceryl dibehenate and Glyceryl behenate

2.3.4.2. **Chemical structure:**

\[
\text{RO}_\text{R} \quad \text{OR}
\]

\[
R = H \text{ or } \text{C}_{22}\text{H}_{43}\text{O}_2
\]

*Figure 15: Chemical structure of Glyceryl behenate*

2.3.4.3. **Molecular Formula:** C_{25}H_{50}O_{4}

2.3.4.4. **Molecular weight:** 414.671 g/mol

2.3.4.5. **Melting point:** 65-77 °C

2.3.4.6. **Appearance:** Fine white powder

2.3.4.7. **Solubility:** Soluble in chloroform and dichloromethane. Insoluble in ethanol, hexane and water
2.3.4.8. Iodine value: 3g I₂/g

2.3.4.9. Saponification value: 145-165 mg KOH/g

2.3.4.10. Odour: Faint odour

2.3.4.11 HLB value: 2

2.3.4.12. Storage conditions: It should be stored in tight container at a temperature less than 35 °C

2.3.4.13. Functional category

- In topical dosage form used as thickening agent for oily phase
- Coating agent, tablet binder, lubricant and viscosity enhancing agent
- In cosmetics used as a skin conditioning agent, emollient, surfactant and emulsifying agent
- Used as ingredient for preparation of lipid nano particles such as solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC).
- Used for modified release oral solid dosage
- Used in coating processes to provide a barrier for the protection of active ingredients

2.3.4.14. Regulatory status

- GRAS listed
- Accepted for use as a food additive in Europe

2.3.5. Pluronic F 68

2.3.5.1. Description:

- It is difunctional block copolymer surfactant terminating in primary hydroxyl groups.
- A nonionic surfactant that is active and non-toxic.

2.3.5.2. Cloud Point: > 100

2.3.5.3. Form: Cast solid

2.3.5.4. Specific gravity: 1.06
2.3.5.5. HLB: > 24

2.3.5.6. Melting point: 52°C

2.3.5.7. Appearance: White powder

2.3.5.8. Solubility: Soluble in water

2.3.5.9. Storage conditions: Store at room temperature

2.3.5.10. Functional category: Non ionic surfactant

2.3.5.11. pH: In 2.5% aqueous solution, between 6.0 - 7.0

2.3.5.11. Critical Micelle Concentration (CMC): 0.04 mM

2.3.6. Tween 80

2.3.6.1. Other name: Polyoxyethylene sorbitan monooleate

2.3.6.2. Molecular Formula: C_{32}H_{60}O_{10}

2.3.6.3. Molecular weight: 604.822 g/mol

2.3.6.4. Appearance: Yellow to orange colour, viscous oily liquid

2.3.6.5. pH: pH of 5% aqueous solution between 6 and 8

2.3.6.6. Solubility: Very soluble in water, soluble in ethanol, cottonseed oil, corn oil, ethyl acetate, methanol and toluene

2.3.6.7. Viscosity: 300–500 centistokes at 25 °C

2.3.6.8. Critical micelle concentration: 0.012mM

2.3.6.9. Storage conditions: It should be stored in a well-closed container and in cool and dark place
2.3.6.10. Application:

- Used as a surfactant in soaps and cosmetics
- Used as a solubilizer such as in a mouthwash
- Used to stabilize aqueous formulations of medications for parenteral administration, and used as an emulsifier

2.3.7. Tween 60

2.3.7.1. Other name: Polyethylene glycol sorbitan monostearate, Polyethylene glycol sorbitan monostearate, Polyoxyethylene sorbitan monostearate

2.3.7.2. Molecular Formula: $C_{64}H_{126}O_{26}$

2.3.7.3. Molecular weight: 1309 g/mol

2.3.7.4. Appearance: Yellow paste

2.3.7.5. Solubility: It is soluble in 40°C water, organic solvents, and insoluble in oil

2.3.7.6. Critical micelle concentration: 27mg/L

2.3.7.7. Storage conditions: It should be stored in cool and dry place

2.3.7.8. HLB: 14.9

2.3.7.9. Application:

- Used as a surfactant for colloidal drug delivery systems
- Also used for targeted drug delivery
2.3.8. Span 80

2.3.8.1. Other names: Sorbitan monooleate, emulsifier S80

2.3.8.2. Molecular Formula: C_{24}H_{44}O_{6}

2.3.8.3. Molecular weight: 428.6

2.3.8.4. Appearance: Pale yellow liquid

2.3.8.5. Saponification value: 145-160 mg KOH/g

2.3.8.6. HLB value: 4.3

2.3.8.7. Storage conditions: It should be stored in cool and dry and place

2.3.8.8. Solubility: It is insoluble in water and soluble in organic solvents

2.3.8.9. Functional category: Non-ionic surfactant

2.3.8.10. Applications: Used as emulsifier, solubilizer, stabilizer, softener, anti-static agent for pharma, cosmetics and textiles industries

2.3.9. Carbopol 980

2.3.9.1. Chemical name: Polyacrylic acid, it is a cross linked polyacrylate polymer

2.3.9.2. Physical state: Solid

2.3.9.3. Solubility: It will swell in water

2.3.9.4. Odour: Slightly acidic

2.3.9.5. Appearance: White solid powder

2.3.9.6. Stability: stable under normal conditions

2.3.9.7. Functional category: Acrylic polymer non irritating to skin
2.3.9.8. Applications:

- It can be used in a wide range of personal care products including shampoos, hair styling products, hand and body lotions, and creams.
- It acts as a thickener and it is ideal for formulating clear aqueous and hydroalcoholic gels.
References


22. European Union herbal monograph on Silybum marianum (L.) Gaertn., fructus, 2015 EMA/HMPC/294187/2013 Committee on Herbal Medicinal Products (HMPC)


