5.1. DRUGS AND EXCIPIENTS PROFILE

5.1.1. *Lagenaria siceraria*

- **Drug**: Aqueous extract of *L. siceraria*
- **Botanical term**: *Lagenaria siceraria* (Molina) Standl.
- **Family**: Cucurbitaceae
- **Alternative word**: Ghiya, Lauki, kaddu, Tumri, Shorakkai
- **Habitat**: Asia, Africa, America
- **Chemical constituents**: Cucurbitacins B, D, G, H, glycosides flavone-C, campesterol and fucosterol

5.1.2. *Ocimum gratissimum*

- **Drug**: Methanolic extract of *Ocimum gratissimum*
- **Botanical name**: *Ocimum gratissimum* Linn.
- **Family**: Lamiaceae
- **Synonyms**: Vriddhitulsi, Ramatulsi, Banjere, Nimmatulsi
- **Habitat**: Tropical Africa, South America, Asia and Nigeria
- **Chemical constituents**: monoterpenes, sesquiterpenes, a-thujene, a-pinene, a-copaene, p-cymene, estragole, thymol, carvacrol

5.1.3. *Moringa oleifera*

- **Drug**: Aqueous extract of *Moringa oleifera*
- **Botanical name**: *Moringa oleifera* L.
- **Family**: Moringaceae
- **Synonyms**: Sahijana, Sobhanjana, Bahola, Salapatra, Sigru
- **Habitat**: Pakistan, Afghanistan, Bangladesh and India
  - Himalayan tract
- **Chemical constituents**: Benzyl isothiocyanate, Niazirin, niaziminin A, niaziminin B, niazimicin, pterygospermin
5.1.4. Wool Fat

Nonproprietary names : BP: Wool Fat, JP: Purified Lanolin
USP: Lanolin, PhEur: Wool Fat

Alternative names : Adeps lanae, E913, lanolina, cera lanae, Protalan
anhydrous, purified lanolin, refined wool fat, lanolin anhydrous

Biochemical name : Anhydrous lanolin

CAS : [8006-54-0]

Experimental formula : It contains NMT 0.25% w/w of H₂O and may
contain up to 0.02% w/w of antioxidant.

Molecular weight : ----- 

Physical formula : ---

Purposeful group : Emulsifying agent; ointment base.

 Uses : Hydrophobic vehicle for ointments and creams

Description : Pale yellow-colored, unctuous substance waxy in
nature. It possesses odour characteristic and faint. It
is a transparent, yellow fluid when melted

5.1.5. Hard paraffin

Nonproprietary names : BP: Hard Paraffin, PhEur: Paraffin, Hard
JP: Paraffin, USP-NF: Paraffin

Alternative names : Paraffinum durum, paraffin wax, paraffinum
solidum, Hard wax.

Biochemical name : Paraffin

CAS number : [8002-74-2]

Experimental formula : CₙH₂ₙ₊₂

Molecular weight : -----

Physical formula : ---

Purposeful group : Ointment base; stiffening agent.

Uses : Component of creams and ointments
Description: Odorless, tasteless, dull, or translucent white compact. Considerably greasy. It burns with a luminous, sooty flame, slight odor may be apparent when melted.

5.1.6. Cetostearyl alcohol

Nonproprietary names:
- BP: Emulsifying Wax
- Ph Eur: Cetostearyl Alcohol (Type A), Emulsifying
- Ph Eur: Cetostearyl Alcohol (Type B), Emulsifying

Alternative names:
- Lanette W, Collone HV, Cyclonette Wax, Lanette SX, Crodex A.

Biochemical name: Anionic emulsifying wax

CAS: [8014-38-8]

Experimental formula: Cetostearyl alcohol (type A), emulsifying contains a minimum of 80% cetostearyl alcohol and 7% sodium cetostearyl sulfate. Cetostearyl alcohol (type B), emulsifying contains a minimum of 80% cetostearyl alcohol and 7% sodium lauryl sulfate

Purposeful group: Emulsifying agent; solubilizing agent; stiffening agent.

Uses: As an emulsifying agent in cosmetics and topical pharmaceutical formulations.

Description: Almost white or pale yellow colored flakes, waxy in nature which when warmed become plastic before melting. Anionic emulsifying wax has a faded characteristic aroma and a weaksense of taste.

5.1.7. White soft paraffin

Nonproprietary names: Petrolatum and lanolin alcohols

Alternative names: Amerchol CAB, petrolatum and wool alcohols,
Forlan 500, Vilvanolin CAB, white soft paraffin and lanolin alcohols, yellow soft paraffin and lanolin alcohols.

**Biochemical name and CAS registry number**
- Petrolatum [8009-03-8] and Lanolin alcohols [8027-33-6]

**Experimental formula and molecular weight**
- A mixture of petrolatum and lanolin alcohols.

**Physical formula**
- 

**Purposeful category**
- Emollient; ointment base; plasticizer.

**Uses**
- As an ointment base in cosmetics and topical pharmaceutical formulation

---

### 5.1.8. PEG 4000

**Nonproprietary names**
- JP: Macrogol 4000, BP: Macrogols, PhEur: Macrogols, USP-NF: Polyethylene Glycol

**Alternative names**
- Pluriol E, Carbowax Sentry, Carbowax, Lipoxol, Lutrol E, macrogola, PEG.

**Biochemical name**
- β-Hydro-α-hydroxy(polyoxy-1,2-ethanediyl)

**CAS number**
- [25322-68-3]

**Experimental formula and molecular weight**
- HOCH₂(CH₂OCH₂)mCH₂OH

**Physical formula**
- ![PEG 4000 Structure](image)

**Purposeful group**
- Base for semisolids; plasticizer; as a solvent; base for pessaries, suppository; As lubricant in solid formulations.

**Uses**
- Excipient in parenteral, topical, ophthalmic, oral, and rectal preparations. Ointment base.
5.1.9. PEG 400

Nonproprietary names: PhEur: Macrogols
JP: Macrogol 400
USP-NF: PEG
BP: Macrogols

Alternative names: Pluriol E, Carbowax Sentry, Carbowax, Lipoxol, Lutrol E, macrogola, PEG.

Biochemical name: α-Hydro-ɷ-hydroxypoly(oxy-1,2-ethanediyl)
CASnumber: [25322-68-3]
Experimental formula and molecular weight: HOCH₂(CH₂OCH₂)ₘCH₂OH

Purposeful group: Base for semisolids; plasticizer; as a solvent; base for pessaries, suppository; As lubricant in solid formulations.

Uses: Excipient in parenteral, topical, ophthalmic, oral, and rectal preparations. Ointment base.

Description: Polyethylene glycol 400 are liquid at ambient temperatures. PEG 400 are off-white to white color, and array in steadiness from waxy flakes to pastes. They have a faded, sweet-smellingscent.
yellow-colored or colorless, viscid fluids.

5.1.10. Sorbitol monooleate

Nonproprietary names : BP: Sorbitan Oleate, JP: Sorbitan Sesquioleate
PhEur: Sorbitan Oleate, USP-NF: Sorbitan Monooleate

Alternative names : Ablunol S-80, Armoten MO, Crill 50, Glycomul O, Hodag SMO, Liposorb O

Biochemical name : (Z)-Sorbitan mono-9-octadecenoate

CAS number [1338-43-8]

Experimental formula : $C_{24}H_{44}O_6$

and molecular weight 429

Physical formula : $R = (C_{17}H_{33})COO$

Purposeful group : Dispersing and emulsifying agent, nonionic surfactant, solubilizing mediator, suspending mediator, wetting mediator.

Uses : Emulsifying agent, solubilizing agent, wetting agent.

Description : Yellow viscous liquid

5.1.11. Liquid paraffin

Nonproprietary names : PhEur: Paraffin, Liquid
JP: Liquid Paraffin
USP: Mineral Oil
BP: Liquid Paraffin
Alternative names : Drakeol, paraffinum liquidum Avatech
Biochemical name : Mineral oil
CAS number [8012-95-1]
Experimental formula and molecular weight : It is a consolidation of refined liquefied soaked cyclic hydrocarbons and aliphatic (C14 –C18) and gained from petroleum
Physical formula :  
Purposeful group : Emollient; lubricant; oleaginous vehicle; solvent; vaccine adjuvant.
Uses : Excipient in topical pharmaceutical excipient
Description : viscid oily fluid, transparent, colorless, deprived of fluorescence in sunlight. Tasteless and unscented

5.1.12. White beeswax
Nonproprietary names : USP-NF: White Wax
JP: White Beeswax
PhEur: Beeswax, White
BP: White Beeswax
Alternative names : ; Cera alba, E901, Bleached wax.
Biochemical name : White beeswax
CAS number [8012-89-3]
Experimental formula and molecular weight : It comprises of 70–75% of a blend of different esters of monohydric alcohols with even carbon ties from C 24 to C36
Physical formula :  
Purposeful group : Controlled-release agent; stabilizing agent; stiffening agent
Uses : Increases consistency of semisolid preparations
Description : yellow-colored sheets or fine granules, tasteless, white or slightly yellow-colored
5.1.13. Span 60

**Nonproprietary names**: BP: Sorbitan Stearate  
JP: Sorbitan Sesquioleate  
PhEur: Sorbitan Stearate  
USP-NF: Sorbitan Monostearate

**Alternative names**: Ablunol S-60, Capmul S, Crill 3, Glycomul S KFG

**Biochemical name**: Sorbitan mono-octadecanoate

**CAS number**: [1338-41-6]

**Experimental formula and molecular weight**: C_{24}H_{46}O_{6}  
431

**Physical formula**:

\[ \text{R} = (\text{C}_{17}\text{H}_{35})\text{COO} \]

**Purposeful group**: Dispersing mediator, emulsifying mediator, nonionic surfactant, solubilizing agent, suspending mediator, wetting mediator.

**Uses**: Emulsifying agent, solubilizing agent, wetting agent.

**Description**: Cream solid

5.1.14. Tween 60

**Nonproprietary names**: BP: Polysorbate 60  
PhEur: Polysorbate 60  
USP-NF: Polysorbate 60

**Alternative names**: Montanox 60, Atlas 70K, Capmul POE-S, Crillet 3, Glycosperse S-20FG
<table>
<thead>
<tr>
<th><strong>Biochemical name</strong></th>
<th>Polyoxyethylene 20 sorbitan monostearate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CAS number</strong></td>
<td>9005-67-8</td>
</tr>
<tr>
<td><strong>Experimental formula and molecular weight</strong></td>
<td>C_{64}H_{126}O_{26} 1312</td>
</tr>
<tr>
<td><strong>Physical formula</strong></td>
<td>-----------</td>
</tr>
<tr>
<td><strong>Purposeful group</strong></td>
<td>Dispersing agent, wetting agent, emulsifying agent, solubilizing agent, suspending agent, nonionic surfactant.</td>
</tr>
<tr>
<td><strong>Uses</strong></td>
<td>Used as emulsifying agents</td>
</tr>
</tbody>
</table>

**5.1.15. Methyl hydroxybenzoate**

<table>
<thead>
<tr>
<th><strong>Nonproprietary names</strong></th>
<th>PhEur: Methyl Parahydroxybenzoate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>JP: Methyl Parahydroxybenzoate</td>
</tr>
<tr>
<td></td>
<td>USP-NF: Methylparaben</td>
</tr>
<tr>
<td></td>
<td>BP: Methyl Hydroxybenzoate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Alternative names</strong></th>
<th>Aseptoform M, 4-hydroxybenzoic acid methyl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ester, Methyl Parasept, Solbrol M</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Biochemical name</strong></th>
<th>Methyl-4-hydroxybenzoate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CAS number</strong></td>
<td>[99-76-3]</td>
</tr>
<tr>
<td><strong>Experimental formula and molecular weight</strong></td>
<td>C_{8}H_{8}O_{3} 152.15</td>
</tr>
<tr>
<td><strong>Physical formula</strong></td>
<td><img src="image" alt="Methyl-4-hydroxybenzoate structure" /></td>
</tr>
</tbody>
</table>

| **Purposeful group** | Preservative as antimicrobial. |
Uses : Preservative in therapeutic preparations
Description : White, crystalline, odorless, and tasteless powder

5.1.16. Propyl hydroxybenzoate
Nonproprietary names : USP-NF: Propylparaben
                      JP: Propyl Parahydroxybenzoate
                      BP: Propyl Hydroxybenzoate
                      PhEur: Propyl Parahydroxybenzoate
Alternative names : Aseptoform P, CoSept P, 4-hydroxybenzoic acid,
                    Nipagin P, Nipasol M, Solbrol P
Biochemical name : Propyl 4-hydroxybenzoate
CAS number : 94-13-3
Experimental formula : $\text{C}_{10}\text{H}_{12}\text{O}_3$
molecular weight : 180.20
Physical formula : 

Purposeful group : Antimicrobial preservative.
Uses : Anti-microbial preservative in pharmaceutical formulation.
Description : White, crystalline, odorless, and tasteless powder

5.1.17. Hydroxypropyl methyl cellulose
Nonproprietary names : BP: Hypromellose
                      JP: Hypromellose
                      PhEur: Hypromellose
                      USP: Hypromellose
Alternative names : Methocel, Pharmacoat, MetoloseHydroxypropyl
methylcellulose, HPMC, hypromellosum, Tylopur, Tylose MO,

**Biochemical name**: Cellulose hydroxypropyl methyl ether

**CAS number**: 9004-65-3

**Experimental formula and molecular weight**

Physical formula:

\[
\begin{array}{c}
R \text{ equi. to } H, \text{ CH}_3, \text{ or CH}_3 \text{ CH(OH)} \text{CH}_2 \\
\end{array}
\]

**Purposeful group**: controlled-release agent, modified-release agent, mucoadhesive, bioadhesive material

**Uses**: oral, ophthalmic, nasal, and topical pharmaceutical formulations

**Description**: Unscented and no taste, creamy-white to white rubbery or gritty powder

### 5.1.18. Ethylcellulose

**Nonproprietary names**: USP-NF: Ethylcellulose

PhEur: Ethylcellulose

BP: Ethylcellulose

**Alternative names**: E462, Surelease, Ashacel, Ethocel, ethylcellulosum, Aqualon, Aquacoat ECD

**Biochemical name**: Cellulose ethyl ether

**CAS number**: [9004-57-3]

**Experimental formula and molecular weight**

\[
\begin{array}{c}
\text{C}_{12}\text{H}_{23}\text{O}_6(\text{C}_{12}\text{H}_{22}\text{O}_5)_n\text{C}_{12}\text{H}_23\text{O}_5 \\
\end{array}
\]
Physical formula : 

![Chemical structure](image)

**Purposeful group** : Viscosity-increasing agent, coating agent, flavoring agent, tablet filler, tablet binder

**Uses** : Drug release modifier, coating agent, water insoluble film, plasticizer, microencapsulation agent, binder, thickening agent in lotion, gels and creams.

**Description** : Tasteless, white to light tan-colored, free flowing, powder

5.1.19. Span 80

**Nonproprietary names** : BP: Sorbitan Oleate
JP: Sorbitan Sesquioleate
PhEur: Sorbitan Oleate
USP-NF: Sorbitan Monooleate

**Alternative names** : Ablunol S-80, Armotan MO, Crill 50, Glycomul O, Hodag SMO, Liposorb O

**Biochemical name** : (Z)-Sorbitan mono-9-octadecenoate

**CAS number** : [1338-43-8]

**Experimental formula** : $\text{C}_{24}\text{H}_{46}\text{O}_6$
and molecular weight: 429

Physical formula: 

\[
R = (\text{C}_{17}\text{H}_{33})\text{COO}
\]

Purposeful group: Dispersing enhancer, emulsifying enhancer, nonionic surfactant, solubilizing enhancer, suspending enhancer, wetting enhancer.

Uses: Emulsifying agent, solubilizing agent, wetting agent.

Description: Yellow viscous liquid

5.1.20. Menthol

Nonproprietary names: BP: Racementhol
JP: dl-Menthol
PhEur: Menthol, Racemic
USP: Menthol

Alternative names: Hexahydrothymol, 3-p-menthanol; p-menthan-3-ol, racemic menthol, dl-menthol, mentholum racemicum, menthomenthol; mentolis, peppermint camphor

Biochemical name: (1RS,2RS,5RS)-(±)-5-Methyl-2-(1-methylethyl)cyclohexanol

CAS number: 15356-70-4

Experimental formula: \(\text{C}_{10}\text{H}_{20}\text{O}\)

and molecular weight: 156.27
Physical formula:

```
CH3
/ \   \\
|   |  \\
CH3---OH
|   |
\   |
H3C---CH---CH3
```

Purposeful group:
Flavoring agent, therapeutic agent.

Uses:
Flavoring agent or odor enhancer in toiletry, confectionery and pharmaceutical products. Skin penetration enhancer in topical formulations.

Description:
It is a free-flowing or agglomerated powder. Colorless, crystalline powder, or, prismatic, or acicular shiny crystals, fused masses or hexagonal or with a strong characteristic odor and taste.

5.1.21. Propylene glycol

Nonproprietary terms:
- PhEur: Propylene Glycol
- British Pharmacopoeia: Propylene Glycol
- USP: Propylene Glycol
- JP: Propylene Glycol

Alternative names:
Propylenglycolum, 1,2-Dihydroxypropane, methyl ethylene glycol, propane-1,2-diol, methyl glycol.

Biochemical name:
1,2-Propanediol

CAS number:
57-55-6

Experimental formula:
C₃H₈O₂

Molecular weight:
76.09
Physical formula : 

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{OH} \\
\text{OH} & \\
\end{align*}
\]

Purposeful group : Preservative, Antimicrobial, stabilizing agent, plasticizer, cosolvent, humectant, disinfectant, solvent

Uses : As a solvent, extractant, and preservative

Description : PG is a clear, viscid, basically odorless fluid, no color, with a sweet-smelling, somewhat pungent taste like glycerine.
5.2. DEVELOPMENT OF CONVENTIONAL POLYHERBAL SEMISOLID DOSAGE FORM

Polyherbal formulations for the topical use on the skin were manufactured with four general types of ointment bases i.e. hydrocarbon bases, absorption bases, water removal bases and water-soluble bases (Remington et al., 2005)

Ointments are semisolid soft preparation intended for application to the skin and mucous membrane without or without rubbing. Hydrocarbon bases are anhydrous, hydrophobic in nature and insoluble in water. Absorption bases are anhydrous and hydrophilic in nature. They are insoluble in water and upon incorporation of aqueous solution forms w/o type emulsion. Water soluble bases are also called as greaseless ointment bases. It consists of water soluble based and they can be easily washed out with water (Jani, 2009).

The different ingredients used to formulate the preparations were shown in table 28.

5.2.1. Formulation method for TSF-1 (Seth, 2007)

Weigh all ingredients and grate waxy materials and melt in a beaker under continuous stirring. Add weighed quantity of extracts in above molten mass under continuous stirring and allow it to cool under stirring. Transfer the product in wide mouth bottle after cooling.

5.2.2. Formulation method for TSF-2 (Seth, 2007)

Weigh all ingredients and melt in a beaker under continuous stirring. Add weighed quantity of extracts in above molten mass under continuous stirring and allow it to cool under stirring. Transfer the product in wide mouth bottle after cooling.

5.2.3. Formulation method for TSF-3 (Seth, 2007)

Weigh all ingredients and melt in a beaker under continuous stirring. Add weighed quantity of extracts in above molten mass under continuous stirring and allow it to cool under stirring. Transfer the product in wide mouth bottle after cooling.

5.2.4. Formulation method for TSF-4 (Seth, 2007)
Melt cetosteryl alcohol, white bees wax, span 60 and propyl paraben in a beaker on water bath. Dissolve tween 60 and methyl hydroxy benzoate in distilled water in a separate tumbler and heat on a water bath. Add hot aqueous phase to the hot oil phase with constant stirring until cold. The prepared cream was filled the wide mouth bottles and kept for the analysis in future.
5.3. EVALUATION PARAMETERS OF CONVENTIONAL POLYHERBAL SEMISOLID DOSAGE FORM

The following parameters were evaluated for the prepared formulations.

1. Determination of the pH
2. Determination of spreadability
3. Determination of Viscosity
4. Primary skin irritancy studies
5. In-vitro diffusion test
6. Release kinetic study

5.3.1. Determination of the pH (Goyal, 2011):

The measurement of pH of the prepared formulations was checked using pH meter (digital) and pH paper. Weighed quantity of prepared formulation was liquefied in 100 ml of purified water and warehoused for around 2 h and then taken the pH. The results were shown in table 29.

5.3.2. Determination of Spreadability: (Parmar et al., 2009)

Measurement of spreadability efficiency of the prepared product was checked by applying the prepared sample in the middle of 2 slides made up of glass and was flattened to uniform width by employing 1000 gramloads for 5 minutes. Now added 240 g of mass to the load pan of the apparatus. The time taken to disconnect the slides of glass, i.e. the period in which the upper slide travels over the lower slide was taken as a degree of spreadability which is denoted by (s).

\[ S = m \times \frac{1}{t} \]

Wherever
m is the mass tide to the upper slide made of glass
l is the length travelled on the slide made of glass
t = time engaged.

The results were shown in table no. 29.
5.3.3. Viscosity Measurement (Akanksha et al., 2009):

Digital viscometer (Brookfield viscometer - model DV-I+) was taken to accessed the viscidness (in centipoise) of the prepared product. The spindle T-D (spindle code S 94) used for the measurement and was revolved at 2.5, 5, 7.5 and 10 rounds per minutes. The reading obtained, nearby to 100 % force, was taken. Samples were maintained at 30.0 ± 2 °C. The outcomes were exposed in table 29.

5.3.4. Primary Skin Irritancy Studies (Patni et al., 2006):

The rats were alienated into five sets of six rats respectively. A 4 cm² part of the rats dorsal portion was clean and bearded and sponged with alcohol or medical spirit. The measured amount of formulation was applied with applicator over the site. The test destinations were watched for 48 h for edema and erythema after application. The results were shown in table no 30.

5.3.5. In-Vitro Drug Release Study (Shah et al., 1999):

Medication discharge studies were performed In-vitro by utilizing a Franz dissemination cell assembly. The cellulose acetate membrane also known as cellophane membranewas used to perform the release study from the preparations prepared. The cellulose acetate membrane having a pore estimate 0.45 µ was equestrian between the giver and receptor section of the dispersion cell setup. The arranged definition was set on the cellophane layer and roofed with aluminum foil. The receptor compartment of the dissemination cell was loaded with phosphate buffer of 7.4 pH. The whole dispersion get together was altered on amagnetic stirrer with a hot plate. The sample in the receptor compartment was continually and consistently mixed utilizing beads of magnet and the temperature was kept up at 37 °c ± 0.50 °c, in light of the fact that the human skin temperature is 37 °c. The specimens were taken at diverse interval from the receptor chamber of the diffusion cell. The receptor solution was reloaded same volume of pH 7.4 phosphate bufferat everyinterim. After taking out, 0.5 ml 10 % Na₂CO₃and 1 ml reagentFolin-Ciocalteu was added in each sample. After it keeps the volumetric flask in dark for 1 h. After 1 h. adjust the volume of volumetric flask to 10 ml with phosphate buffer. Finally, the absorbance
was taken at 760nm of the solution. Standard curve was developed with dissimilar concentration of gallic acid. The results were shown in table 32 and figure 26 - 30 for all four formulations.

**5.3.6. Drug Release Kinetic Study (Mohammed and Khedr, 2003, Desai and Kumar, 2004):**

To illustrate the discharge phenomenon of active constituents from the prepared dosage forms, the release figures were analyzed using different kinetic models to assess the release of the pattern of the drug from the different types of formulations.

- **Zero order kinetics:** It is presumed that the region does not transformed and no evenness condition attained and can be signified by the

  $$Q_t = Q_o + K_o \cdot t$$

  Whereas $Q_t =$ volume of medicine liquefied in time
  $Q_o =$ primary quantity of medicine in the solvent
  $K_o =$ constant for zero order release.

- **First order kinetics:** For release kinetics of first order, drug dissolution data obtained from the dissolution of the dosage forms were fitted to the equation given below

  $$\log Q_t = \log Q_o + K_1 \cdot t / 2.303$$

  Where $Q_t =$ quantity of medicine release in time
  $Q_o =$ preliminary amount of medicine in solution
  $K_1 =$ constant for first order release

- **Higuchi model:** According to this model, mathematical terminologies were found for medicine units disseminated in an constant matrix acting as the dissemination solvent and expressed as

  $$Q_t = K_H \cdot t^{1/2}$$

  Whereas
  $Q_t =$ quantity of medicine released in $t$ time and
\[ K_{H} = \text{constant for higuchi dissolution.} \]

- **Korsmeyer and Peppas release model:** Conferring the correlation suggested by Korsmeyer and his coworkers, as

\[ \frac{M_t}{M_\infty} = K t^n \]

Where, \( M_t / M_\infty \): slight release of the medicine,

- \( t \): means the release interval,
- \( K \): constant for integrating structural and characteristics geometrical of the instrument
- \( n \): diffusional proponent that characterized release mechanism type during the process of dissolution.

The value of \( n \) will describe the type of kinetics followed by the testing product. The value of \( n \) and it corresponding release kinetics are shown below

- **Higuchi Matrix (Fickian Diffusion)** \( n \) greater or equal to 0.5
- **Anomalous Transport** \( n \) is in between 0.5 – 1.0
- **Zero Order Release (Case-II Transport)** \( n \) is 1
- **Super Case-II transport** \( n \) is greater than 1

Here, the ‘\( n \)’ values were projected by \( \log (M_t/M_\infty) \) of linear regression against \( \log (t) \) of dissimilar products or materials that can be tested to check the release pattern.

This model utilized, when the discharge system is not recognized or when other than one sort of discharge wonder could be included. The results are shown in table 33.
5.4. DEVELOPMENT OF POLYHERBAL TRANSDERMAL PATCHES:

Transdermal drug delivery system or dosage form or TDDS are characterized as independent, discrete measurements structures which, once connected to the in place skin, convey the medications through the skin at a controlled rate to the systemic dissemination. The fundamental preferences of transdermal medication conveyance framework are

- It delivers a study imbue ment of a medication over a delayed time of time in sustained manner.
- It improves the pharmacological significance of numerous medications by dodging particular issues connected with the medication, e.g., gastro-intestinal disturbance, low ingestion, deterioration because of first pass "hepatic" metabolism. (Jain, 2008)

5.4.1. Method of Preparation:

Solvent casting method utilized for obtaining transdermal patches enclosing herbal extracts using cylinder-shaped glass casts. For the development of transdermal patches, different concentrations of polymers alone or in combination were used. Span 80 and menthol is used as permeation enhancer and propylene glycol is used as a plasticizer. Chloroform is used as a solvent. First two formulations are prepared using HPMC alone having drug and polymer ratio i.e. 1:2 and 1:3. Further, two formulations are prepared using HPMC and EC in combination having drug and polymer in ratio 1: (1:2) and 1: (1:3). (Amjad et al., 2011)

Procedure:

Plants extracts of required quantity were weighed and dissolved in chloroform along with span 80 and menthol. This solution was then added to the polymer base, prepared by dissolving polymer and plasticizer in chloroform and stirred continuously to get uniform solution. The chloroform was used to mark up the ultimate bulk of the solution. Definite volume of the above solution was then poured into siliconized glass mold and dried at normal temperature and environment for 24 h. results in obtaining films. The films were then stored in an airtight container. Surgical bandage layer was used as a backing material. The 2 cm² diameter film was cut and stacked on the backing material. To avoid the direct contact of film with the skin it has been covered with a cotton bandage. Finally, the Teflon release liner was applied on it. These patches were then subjected to further evaluation (Arora and Mukherjee, 2002)
* Dose calculation:

The total amount of herbal extracts used in semisolid formulation is 300 mg (i.e. 67 mg of *Lagenaria siceraria*, 33 mg of *Ocimum gratissimum* and 200mg of *Moringa oleifera*). For the preparation of a transdermal patch, 300 mg minimum dose is required. So, the desired dimension of the film is 2 × 1 cm (2cm²) and it should contain 300 mg of extracts. But the area of casting plate is 78.5 cm². If 2 cm² areas of film should contain 300 mg of drug, then 78.5 cm² areas of film will contain 11.775 g drug. Therefore, total amount of drug required to be added in the film casting solution is 11.775 g. The prepared film is separated from the plate and cut in to 2 × 1 cm (2 cm²) which contains required quantity of the extract, 300 mg. The calculation of the dose are given below.

➢ How to get 78.5cm² areas of casting plate?

Area = \( \pi / 4 \times d^2 \)

= 78.5 cm²

Where, \( \pi = 3.14 \),

d= diameter of casting plate (10 cm)

now,

2cm² area contain=300 mg extracts

78.5cm² area contains?????

Therefore, 11.775 g of the mixture of herbal extracts (2.62 g of *Lagenaria siceraria*, 1.23 g of *Ocimum gratissimum* and 7.85 g of *Moringa Oleifera* needed for 78.5cm² areas of casting plate.
5.5. EVALUATION OF POLYHERBAL TRANSDERMAL PATCH (Kumar et al., 2010)

The parameters evaluated for polyherbal transdermal patches are

1. Thickness of patch
2. Folding endurance
3. Percentage moisture content
4. Percentage moisture uptake
5. Tensile strength
6. Skin irritation test
7. In-vitro skin permeation test
8. Release kinetic study

5.5.1. Thickness of Patch:

The width of the prepared patches was assessed by means of a micrometer (digital). The thickness was measured from a different position of the patches which determine the middling width and the SD (standard deviation) for the identical prepared transdermal patch to confirm the thickness uniformity.

5.5.2. Weight Uniformity:

Before testing, the formulated patches are dried for 4 h at 60 °C. A definite zone (3 x 1 cm from the central portion) of the prepared patch is cut down into different parts and weigh in a numerical balance. The normal weight (average) and standard deviation qualities were figured from the individual masses. The results were shown in table 35.

5.5.3. Folding Endurance:

A band of exact size i.e. 2 cm in diameter are uniformly cut down form the prepared patch and repetitively crumpled at the similar point till it cracks. The repetitions of times the film could be collapsed at the same spot without splitting gave the estimation of the folding endurance or collapsing perseverance test.
5.5.4. Percentage Moisture Content:

The strips formulated are weighed independently and held in desiccator having fused of intertwined calcium chloride at normal environment for 24 h. Later, the strips were reweighed and rate dampness substance was resolved from the beneath specified equation.

\[
\% \text{ moisture content} = \frac{\text{initial weight} - \text{final weight}}{\text{final weight}} \times 100
\]

The results were shown in table 35.

5.5.5. Percentage Moisture Uptake:

The mass of transdermal patch that are retained for 24 h in a desiccator containing potassium chloride saturated solution at room temperature in directive to sustain 84% relative humidity. Films were reweighed after 24 h. and percentage dampness content was determined from the beneath specified equation

\[
\% \text{ moisture uptake} = \frac{A - B}{A} \times 100
\]

Where, A = Final weight of the patch

B = Initial patch weight

The outcomes were shown in table no 35.

5.5.6. Tensile Strength:

The stretchable power was determined on the basis of elongation. In this, the prepared strip of polymer was dragged by utilizing a pulley system. In this, loads were progressively putted to the load pot to rise the dragging force till the strip was wrecked. Here, the distance travelled (also known as elongation) by the indicator point before disruption of the strip was noted with the assistance of amplifying glass on the chart paper, the elasticity was computed as kg cm\(^2\). The results were shown in table 35.
5.5.7. Skin Irritation Study:

The albino wistar rats were divided into two sets of six rats. A 4 cm² part of the rats' dorsal region was cleaned, bald, and sponged using alcohol or surgical spirit. Transdermal patches were applied over the site. The test portion were watched for 48 h for erythema signs or edema later application of the prepared formulation and the results were noted down.

5.5.8. Skin Permeation Studies (In-Vitro):

Skin diffusion studies were done by utilizing a Franz dissemination cell assembly with a receptor partition of 22.5 ml limit. The extracted rodent stomach skin (albino wistar) was attached in the middle of the benefactor and receptor section of the Franz assembly. Paraffin film used to cover the patch which placed over the stomach skin in the assembly. The diffusion assembly receptor section was packed with pH 7.4 phosphate buffer. The entire diffusion assembly receptor section was secure on a magnetic agitator, and media in receptor portion was continually and uninterruptedly agitated at 50 rpm by means of beads made of magnet of particular size. The temperature was kept constant at 32 °C with 0.5 °C plus minus deviation during the test. The formulation were taken at diverse time interims from the intake compartment of the dispersion cell. The receptor stage was renewed with an equivalent volume of pH 7.4 phosphate buffer at each one sample taking out. After withdrawal of each sample, 0.5 ml 10 % sodium bicarbonate reagent and 1 ml Folin-Ciocalteu was added. Keep the volumetric flask in dark for 1 h. After 1 h. adjust the volume of volumetric flask to 10 ml with phosphate buffer. Finally, the absorbance of the test sample was taken at 760 nm wavelength. A standard graph was made with dissimilar concentration of gallic acid. The results are shown in table 37.

5.5.9. Drug release kinetic study (Mohammed and Khedr, 2003, Desai and Kumar, 2004):

To illustrate the discharge phenomenon of active constituents from the prepared dosage forms, the release figures were analyzed using different kinetic models to assess the release of the pattern of the drug from the different types of formulations.
• **Zero order kinetics:** It is presumed that the region does not transformed and no evenness condition attained and can be signified by the

\[ Q_t = Q_o + K_o t \]

Whereas \( Q_t \) = volume of medicine liquefied in time
\( Q_o \) = primary quantity of medicine in the solvent
\( K_o \) = constant for zero order release.

• **First order kinetics:** For release kinetics of first order, drug dissolution data obtained from the dissolution of the dosage formswere fitted to the equation given below

\[ \log Q_t = \log Q_o + K_1 t /2.303 \]

Where \( Q_t \) = quantity of medicine release in time
\( Q_o \) = preliminary amount of medicine in solution
\( K_1 \) = constant for first order release

• **Higuchi model:** According to this model, mathematical terminologies were found for medicine units disseminated in an constant matrix acting as the dissemination solvent and expressed as

\[ Q_t = K_H . t^{1/2} \]

Whereas
\( Q_t \) = quantity of medicine released in time and
\( K_H \) = constant for higuchi dissolution.

• **Korsmeyer and Peppas release model:** Conferring the correlation suggested by Korsmeyer and his coworkers, as

\[ M_t / M_\infty = Kt^b \]
Where, $M_t / M_\infty$: slight release of the medicine,

- $t$: means the release interval,
- $K$: constant for integrating structural and characteristics geometrical of the instrument
- $n$: diffusional proponent that characterized release mechanism type during the process of dissolution.

The value of $n$ will describe the type of kinetics followed by the testing product. The value of $n$ and it corresponding release kinetics are shown below

- Higuchi Matrix (Fickian Diffusion) \( n \) greater or equal to 0.5
- Anomalous Transport \( n \) is in between 0.5 – 1.0
- Zero Order Release (Case-II Transport) \( n \) is 1
- Super Case-II transport \( n \) is greater than 1

Here, the ‘$n$’ values were projected by $\log (M_t / M_\infty)$ of linear regression against $\log (t)$ of dissimilar products or materials that can be tested to check the release pattern.

This model utilized, when the discharge system is not recognized or when other than one sort of discharge wonder could be included. The results are shown in table 38.
5.6. ANTI-INFLAMMATORY SCREENING OF FORMUALTIONS

5.6.1. Anti-Inflammatory Activity of Conventional Polyherbal Semisolid Formulations:

Animal assortment:

Animals (albino rats) of whichever gender weighing 150 to 250 g were carefully chosen for testing of the polyherbal formulation prepared. The experimental creatures were alienated into six clusters, each cluster having six rats. The comforter material of the cart was altered each day.

Materials:

a. Formulation TSF-1
b. Formulation TSF-2
c. Formulation TSF-3
d. Formulation TSF-4
e. Standard: Hydrocortisone ointment (1%)
f. Carrageenan (Sigma Chemicals Co., USA) 0.1 ml of 1% solution.
g. Plethysmometer (UGO Basile 7141)

Method: (Calvo, 2006)

For assessing of anti-inflammatory potential of topical semisolid preparations, 0.3 g of prepared polyherbal ointment of the plants extract were tested to the plantar surface of the left rear paw by delicately rubbing 50 repetitions with the pointer. Rats gatherings of the control got dummy ointment i.e. only base of ointment. As a reference, hydrocortisone (1%) drug ointment was used. Percentagesuppression of swelling was determined by

\[
\text{Inhibition \%} = (1 - \frac{EC}{ET}) \times 100
\]

In the above equation ‘EC’ signifies control group edema volume and ‘ET’ signifies treated group edema volume with prepared polyherbal formulation.
5.6.2. Anti-Inflammatory Activity of Polyherbal Transdermal Patch:

Animal assortment:

Animals (albino rats) of whichever gender weighing 150 to 250 g were carefully chosen for the testing of the prepared transdermal patches. Albino rats were alienated into three clusters, each cluster contains six rats. The bedclothes material of the barred enclosure was changed each day.

Materials:

a. Formulation TP-4
b. Standard: Diclofenac sodium. (INAC injection, Zydus Recon, India)
c. Carrageenan (Sigma Chemicals Co., USA) 0.1 ml of 1% solution.
d. Plethysmometer (UGO Basile 7141)

Method:

Albinowistar rats were distributed into three different sets (n=6) and were supplied with free admittance to water and foodstuff. The experimental rats were held under perception for 24 h. The stomach side of rats was shaved before 12 h from the beginning of the trial. The transdermal strip was connected on the clean-shaven backs of rats of all clusters. First cluster assisted as control and second cluster received the drug diclofenac as the standard. Right rear paw edema was induced in all bunches of rats by subplanter infusion of 0.1 ml homogeneous suspension of carrageenan (1% w/v in normal saline). In the rats of group 1, 2 and 3, carrageenan was infused after 30 minutes. The swelling of the infused paw was assessed promptly and at 0.5, 1, 2, 3 and 4 h. time interval with a plethysmometer after dose. The volume of paw swelling was resolved now and again and communicated as % edema in respect to the starting rear paw volume (Shah and Seth, 2010). Percent inhibition of swelling was measured by,

\[
\text{% inhibition} = \frac{1 - \frac{vt}{vc}}{\frac{vt}{vc}} \times 100
\]

Whereas ‘vc’ symbolizes controlled groupedema volume and ‘vt’ symbolizes treated groupedema.
5.6.3. Statistical Analysis

Information were communicated as mean ± SEM (standard error mean). Information were examined by utilizing examination of change took after by Dunnett's t-test. Contrasts were thought to be huge at P < 0.05.
5.7. STABILITY STUDY OF FORMULATIONS AS PER THE ICH GUIDELINES

5.7.1. Stability Study of Conventional Polyherbal Semisolid Formulations:

The reason of stability assessment is to give a sign on how the nature of medication material or medication item contrasts with time under the impact of a mixture of natural variables, for example, temperature of nature's domain, moisture and light. It is additionally used to make a re-test period for the medication substance or a time span of usability for the medication item and proposed stockpiling environments. The storage condition used for stability studies are 25.0°C, 40°C, 60°C with ± 2°C deviation and 60 % RH, 75 % RH, 80 % RH with ± 5 % deviation respectively.

Stability studies were carried out all formulations stored in sealed amber coloured glass bottle lined internally with aluminum foil. These were stored at 25.0°C, 40°C, 60°C with ± 2°C deviation for 6 months and 60 % RH, 75 % RH, 80 % RH with ± 5 % deviation respectively for four weeks (Guideline, 2003)

All products were assessed regarding physical progressions like progressions in color, smell, pH and phase separation, thereby disturbing their consistency and other wanted properties (Chakole et al., 2009)

5.7.2. Stability Study of Polyherbal Transdermal Patch Formulation:

Stability studies are directed conferring to the guidelines of ICH by loading the transdermal patches of optimized formulation at 40 °C and 75 % with ± 0.5 °C and 5 % RH deviation for 6 months. The sample of product were taken at 0, 30, 60, 90, 120 and 180 days and investigate for the various physicochemical parameters (Guideline, 2003)