Formulation and Evaluation of Proniosomal Transdermal Gel of Dithranol

INTRODUCTION:

Skin

Skin is largest protective organ of human body which has covered about 2- square meter area of body. Confide covering of skin is very densely cross linked structure of proteinWhich have decreases absorption of drug in to the cells. (Maya W. et al., 2012).

Skin of human is most significant and targeted area/site for treatment of local skin diseases. Skin act as rate limiting barrier for entering or penetrating of drugs in body. There are a lot of approaches or method for penetration enhancement across the skin. In which vesicular and provesicular is one of them most promising system fulfils of this requirement. (Touitou E, et al.,2000), (Jain S,et al.,2003)

Transdermal systems provide supply of drug in skin in controlled manner and avoid oral disadvantages. Many anti-inflammatory and analgesic drugs which are used for osteoarthritis and rheumatoid arthritis are prepared as transdermal because these drug cause lot of adverse effects, mainly GIT disturbances such as irritation and ulceration. These types of drugs have short lives in blood. (Bhargava T. et al, 2011).

PSORIASIS
Psoriasis is a chronic, long life, skin disease in which body immune system is mainly responsible. It is characterized by hyper proliferation of keratinocytes. (Saraceno R., et al 2008). Psoriatic patient suffers from inflammation, local itching with pain in affected area. Sometimes approx. more than or up to 40-50 % of psoriatic patient associated with psoriatic arthritis which involves joint pain and swelling in joints. (Gordon K.B., 2006; Racz, E.2009; Clark, A.R.2000)


Different types of systemic and topical treatment of psoriasis are available in present time but its treatment is totally dependent on following nature of disease. (Menter A, et al.,2007)

a) Severity  
b) Cost of drug and Convenience of patient  
c) Relevant –co-morbidities  
d) Effectiveness  
e) Individualization of patient response.
## MANAGEMENT OF PSORIASIS IN NORMAL PRACTICE

<table>
<thead>
<tr>
<th>Delivery System</th>
<th>Drugs</th>
<th>Efficacy/Safety</th>
<th>Main side effects</th>
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</thead>
<tbody>
<tr>
<td><strong>Topical</strong></td>
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<tr>
<td>a) Corticosteroids</td>
<td>Clobetasol 0.05% Betamethsone valerate 0.1%</td>
<td>Low potency to very potent/safe when use short period</td>
<td>Skin atrophy</td>
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<tr>
<td>b) Chrysarobin derivative</td>
<td>Dithranol (Anthralin)</td>
<td>Moderate to severe psoriasis (Short contact regimen)</td>
<td>Local irritation, Staining</td>
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<tr>
<td>c) Vitamin D and these analogs</td>
<td>Calcitriol, Calcipotriol, Tacalcitol</td>
<td>More effective when use combination with other</td>
<td>Irritation and Burning sensation, More expensive</td>
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<tr>
<td><strong>Systemic</strong></td>
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<tr>
<td>a) Immunosuppressive</td>
<td>Methotrexate, Cyclosporine</td>
<td>Less effective/ sometime Organ-toxicity</td>
<td>Hepatotoxicity, Folate deficiency,</td>
</tr>
<tr>
<td>b) Calcineuriun inhibitor</td>
<td>Tacrolimus, Pimecrolimus</td>
<td>Limited because size of molecules, low skin penetration</td>
<td>Malignancy, Itching, Stinging etc.</td>
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<td><strong>Radiation</strong></td>
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<tr>
<td>a) Phototherapy</td>
<td>Ultraviolet B (UVB) combined with Either coal tar or dithranol</td>
<td>Scalp psoriasis</td>
<td>Pruritus, headaches</td>
</tr>
<tr>
<td>b) Photochemotherapy</td>
<td>UVA (long wave) combined with Psoralen, Methtreaxate, Etretinate etc.</td>
<td>Notable decrease in erythema, scaling</td>
<td>Cancer risk, Folate deficiency, Liver enzymes level elevated</td>
</tr>
</tbody>
</table>

## NOVEL DRUG DELIVERY SYSTEM

Different methods are recently used for novel drug delivery system such as vesicular (liposomes, niosomes) and provasicular (proniosomes, Aquasomes ethamosomes etc.), nanoparticles, microsphere etc

### VESICULAR SYSTEM

### NIOSOMES:

Niosomes is one type of non ionic surfactant vesicles which are prepared by admixture of non ionic surfactant, phosphate and cholesterol with subsequent hydration in hydrophilic media.
Cholesterol works as stabilizing agents which have been used for preparation of niosomes. (Singh C.H., et al., 2011). Niosomes may work as a depot of drug and release the drug in sustained or controlled manner. It consists of amphiphilic moieties which provide a wide solubility range. (Dhiman S., et al., 2012).

**DISADVANTAGES** (Agarwal A., et al., 2012)
1. On storage they aggregate with each other.
2. Whenever it’s taken orally, bile salts and phospholipase enzyme of body act against this formulation.
3. Limited hydrolysis and leakage properties of drugs.

**PROBLEM WITH VESICULAR SYSTEM**

![Diagram showing disadvantages](image)

**PROVESICULAR SYSTEM**

**PRONIOSOMES GEL**

Proniosomes gel is liquid crystal laminar structure which is made up of surfactant, cholesterol and lecithin. It is a very popular because it is easy to apply and absorption via skin is also better than other preparation of semisolids (e.g. ointment, cream). It is a drug preparation which can be converted in to niosomes by hydration. (Ram A., et.al., 2012). Surfactants are mainly employed for coating of proniosomes. (Malakar J.,et al 2011).

**ADVANTAGES OF PRONIOSOMES GEL.** - (Singla S., et al., 2012)
1. Bioavailability and permeation of drug is enhanced.
2. Transdermal/Topical preparation of drug delivery system can be developed by proniosomal preparation.
3. Physically (aggregation, fusion, leaking) and chemically they are more stable than niosomes and liposome.

4. It is having an optical flexibility, packaging and processing are very easy than conventional vesicular system.

5. Do not require any special storage and handling condition.

6. Improved biocompatibility, non immunogenicity and non toxicity.

7. Improved permeation of drug via skin with protection of drug with biological components.

8. Release of drug in sustained or controlled pattern.

**DRUG PROFILE**

Dithranol IP (anthralin ; Dioxyanthranol )

![Chemical Structure of Dithranol](image)

**Chemical name**------ 1, 8-Dihydroxy-9(10H)-anthracenone

**Molecular formula**  \( \text{C}_{14}\text{H}_{10}\text{O}_{3} \)  \( \text{MW} = 226.23 \)

**Category**—Topical anti psoriatic, **Description:** yellow or orange yellow microcrystalline powder

**Mechanism of action of Dithranol:-**

a) Inhibition of cell proliferation. *(Kemeny L., 1990).*

b) Inhibition of granulocyte function. *(Ternowitz T., 1987).*

c) Suppression of immune system. *(Anderson R., 1987).*

d) DNA duplication and repairment. *(Muller, K., 1995).*

e) Inhibit e- transport chain and G6PD. *(Fuchs J., -1990), (Cavey D., 1981).*