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Research Article

ASSESSMENT OF ANTI-PSORIASIS-ANTI-INFLAMMATORY-ANESTHETIC COMBINATION AS A THERAPY IN PSORIASIS, ECZEMA, RINGWORM INFECTION ASSOCIATED WITH MINIMIZE THE SIDE EFFECTS OF DITHRANOL

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ABSTRACT

Skin diseases are the common infectious diseases in human. Existing combination of Dithranol & salicylic acid is available in the market in India. (Ointment Ringozone(R)) A stiff dithranol 0.5% ointment shows colour changes, degradation and loss of potency after adverse storage. Varying strength of salicylic acid were added in an attempt to protect the dithranol. The most common corticosteroids used topically for anti-inflammatory activity . Indication of Betamethasone valerate are anti-inflammatory, on eczema, psoriasis. Lignocaine hydrochloride produces local anesthetic effect which will reduces irritation and burning sensation of skin. Also the Betamethasone valerate and Lignocaine HCL combine given in dental anesthetics. The most commonly used treatment for all types of hyperpigmentary disorders is topical hydroquinone. Corticosteroids are also given with hydroquinone in hyperpigmentation during healing step. Salicylic acid is a widely used keratolytic agent in the treatment of hyperkeratosis conditions such as

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psoriasis, eczema. Petrolatum containing 10% salicylic acid is a commonly used ointment for this purpose.

KEY WORDS: Dithranol, Psoriasis, Eczema.

INTRODUCTION

Skin diseases are the common infectious diseases in human. Skin diseases like Eczema/dermatitis, ringworm infection/dermatophytes and Psoriasis are most common skin infectious diseases.

Eczema is a heterogeneous group of different non-infectious skin diseases which may be caused by irritative as well as immune mechanisms and lead to pathological changes in the epidermis and upper dermis

Dermatophytes are types of fungi that cause common skin, hair and nail infections. Infections caused by these fungi are also known by the names "tinea" and "ringworm."

Psoriasis is common chronic skin disease, which course is unpredictable. A large area of the body can be covered with psoriasis lesions.

- Psoriasis is an erythematosquamous skin disorder.
- Psoriasis is characterized by cutaneous inflammation and epidermal hyper proliferation.

PREVALENCE

- **Eczema**

  According to statistics 15-25% of all dermatological patients suffer from eczema.

- **Ringworm**

  From Statistic 5-8 % of all dermatological patient suffer from dermatophytes.

- **Psoriasis**

  Affects 1% to 3% of the population worldwide.

FINDING OF PROBLEM

Topical Treatments

Vit D : Hyper calcaemia
Corticosteroids: Tachyphylaxis.
Dithranol : Irritation, Burning of skin & it causes itching , Inflammation, Hyper pigmentation.
Among this Dithranol are most frequently used in the market. (Ringozone [R])
Exist Marketed Formulation.
Dithranol 0.5 %w/w

Salicylic Acid 10.0 % w/w
Ointment Base q.s.

The present research work investigate To minimize the side effects of existing topical formulation which are used in skin diseases, by developing novel topical formulation for skin diseases.

To evaluate physical as well as chemical compatibility of Dithranol, Salicylic acid, Betamethasone valerate, Lignocaine hydrochloride, Hydroquinone

1. To formulate Topical formulation by selecting compatible base and method of formulation.
2. To evaluate the prepared topical formulations by standard methods of evaluations.
3. To evaluate & compare the local anesthetic activity of prepared formulation by infiltration anesthesia in guinea pigs.
4. To evaluate & compare the anti-inflammatory activity of prepared formulation by Carrageenan induces paw edema in Rat.
5. To evaluate & compare the Anti-psoriasis activity of prepared formulation by Normal animal model for psoriasis/ Mouse tail test for psoriasis.
6. To evaluate & compare the skin lightning activity of prepared formulation by using black guinea-pig.

MATERIALS AND METHODS

- **Determination of Physical and Chemical stability of Drugs :**

The (Physical and Chemical stability of Dithranol, Betamethasone Valerate, Salicylic acid, Lignocaine Hcl, Hydroquinone. were determined.

- **Formulate topical preparations.**
  - Drugs compatible base was selected.

    Paraffin ointment base.

    White Beeswax 20 gm
    Hard Paraffin 30 gm
    Cetostearyl alcohol 50 gm
    White soft paraffin 900 gm

- Suitable method of preparation was selected.

  All Bases was melted and according to the descending order of melting point of Drugs are mixed.

- **Formulate topical preparations.**

Dithranol	0.5%
Betamethasone valerate	0.1%
Salicylic acid	10.0%
Hydroquinone	2.0%
Lignocaine HCL	5.0%
Ointment was prepared.	Q.s.

➢ **Evaluations of topical preparation.**

- Different types of parameters was evaluated for topical formulation

Physical Evaluation.

- Colour
- Appearance
- Feel on application

Subjective Properties.

- Consistency
- Texture

pH of topical Formulation.

➢ **Topical preparation was selected for further pharmacological study.**

➢ **Evaluation of the local anesthetic activity.**

It was carried-out by infiltration anesthesia in guinea pig.

1 Group Combination

2 Group Lignocaine HCL 5% w/w ointments.

3 Group Control

Shaved the back area of guinea pig near 4 to 5 cm in circle and leave it for 24 hours. For reducing the irritation. Ointment was applied and reading was taken after 5 minutes up to 30 min. by pricking the

zone at 3 to 5 sec. intervals, in each 5 min. 6 pricks was given. Anesthesia was shown in fails of pricking response by guinea pig.

- **Evaluation of the anti-inflammatory activity.**

It was carried-out by Carrageenan induce paw edema in Rat.

Containing 5 groups each of 6 animals.

1 Group Combination.

2 Group Betamethasone valerate

3 Group Salicylic acid

4 Group B. V. + S. A.

5 Group Control

Male or female rats with a body weight between 100 and 150 g are used. The animals are fasting overnight. To insure uniform hydration, the rats receive 5 ml of water by stomach tube (controls) or the test drug dissolved or suspended in the same volume. Thirty minutes later, the rats are challenged by a subcutaneous injection of 0.05 ml of 1% solution of carrageenan into the plantar side of the left hind paw. The paw is marked with ink at the level of the lateral malleolus and immersed in mercury up to this mark. The paw volume is measured plethysmographically immediately after injection, reading were taken up to 3 hr. by applying ointment.

- **Evaluation of the Anti-psoriasis activity.**

It was carried-out by Mouse tail model for psoriasis.

Containing 5 Group each of 10 Animals.

Group 1Combination

Group 2 Dithranol

Group 3 Betamethasone valerate

Group 4 B.V. + Dithranol

Group 5 Control

On normal mice tail drug was applied the contact time was 2 hr. and 3 time in day it was applied for 3 weeks.

- **Evaluation of the skin lightning activity.**

It was carried-out by Depigmentation method using black guinea pig.

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Containing 5 groups each of 3 animals.

Group 1Combination

Group 2 Hydroquinone

Group 3 Betamethasone valerate

Group 4B.V. + Hydroquinone

Group 5 Control

The preparation was applied to the left ear of each guinea pig and compared with Right ear. Visual inspection was done for compared.

RESULTS

1. **Evaluation of topical Preparation**

Physical Evaluation.

Sr. No.	Physical Parameter	Formulation
1	Colour	Yellow
2	Appearance	Greasy
3	Feel on application	Smooth

Subjective Properties.

Sr. No.	Parameter	Formulation
1	Consistency	Good
2	Texture	Smooth

pH of ointment.

pH of formulation	Time in Days						
	0	2	4	7	14	22	30
	6.30	6.35	6.35	6.30	6.30	6.30	6.30

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2. Evaluation of local anesthetic activity.

OBSERVATION TABLE

2.1 Control

Animal	5 min		10 min		15 min		20 min		25 min		30 min		average	
	+	-	+	-	+	-	+	-	+	-	+	-	+	-
1	6	0	6	0	6	0	6	0	6	0	6	0	36	0
2	6	0	6	0	6	0	6	0	6	0	6	0	36	0
3	6	0	6	0	6	0	6	0	6	0	6	0	36	0
													108	0

% of anesthesia produced in control group was 0 %

2.2 Standard

Animal	5 min		10 min		15 min		20 min		25 min		30 min		average	
	+	-	+	-	+	-	+	-	+	-	+	-	+	-
1	3	3	0	6	0	6	0	6	0	6	0	6	3	33
2	5	1	1	5	0	6	0	6	0	6	1	5	7	29
3	6	0	1	5	0	6	0	6	0	6	0	6	7	29
													17	91

% of anesthesia produced in Standard group was 84.25 %

2.3 Test

Animal	5 min		10 min		15 min		20 min		25 min		30 min		average	
	+	-	+	-	+	-	+	-	+	-	+	-	+	-

1	**4**	**2**	**0**	**6**	**0**	**6**	**0**	**6**	**0**	**6**	**1**	**5**	**5**	**31**
2	**4**	**2**	**0**	**6**	**0**	**6**	**0**	**6**	**0**	**6**	**2**	**4**	**6**	**30**
3	**5**	**1**	**0**	**6**	**0**	**6**	**0**	**6**	**0**	**6**	**2**	**4**	**7**	**29**
													18	**90**

% of anesthesia produced in Test group was 83.33 %

- **Table 2.3 shows equivalent result to that of Table 2.2.**

3. **Evaluation of anti-inflammatory activity.**

Table 3.1 Anti-inflammatory activity

Time In Min	**Control**	**Combination**	**B.V.**	**S.A**	**B.V. + S.A.**
0	0.02±0.02	0.02±0.02	0.02±0.02	0.02±0.02	0.02±0.02
30	0.42± 0.025	0.32± 0.02	0.34± 0.01	0.34± 0.03	0.33± 0.01
60	0.47± 0.02	0.28± 0.01	0.30± 0.02	0.30± 0.02	0.29± 0.03
90	0.54± 0.02	0.23± 0.02	0.26± 0.04	0.24± 0.01	0.24± 0.02
120	0.58± 0.02	0.15± 0.01	0.16± 0.02	0.17± 0.02	0.16± 0.01
150	0.64± 0.02	0.05± 0.005	0.07± 0.01	0.06± 0.02	0.05± 0.01
180	0.65±0.02	0.01± 0.01	0.05± 0.01	0.02± 0.02	0.01± 0.01

± SEM

Table 3.1 Shows the oedema control in B.V.+S.A. was equivalent to that of the oedema control in combination.

4. **Evaluation of Anti psoriatic activity. Table 4.1**

Table 4.1 Anti psoriatic activity

Treatment	**Orthokeratosis %**	**Activity %**	**Change in epidermal**

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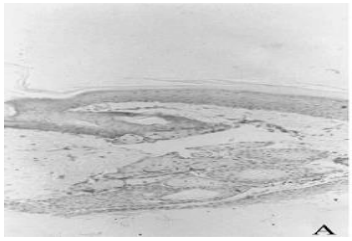
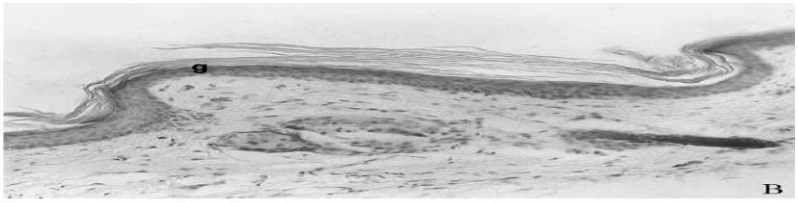
			thickness (%)
Combination	**75.6 ± 3.1**	**66.5**	**5**
Dithranol	**67.0 ± 3.4**	**54.7**	**7**
Betamethasone Valerate	**60.0 ± 2.4**	**45.2**	**6**
B.V. + Dithranol	**53.2 ± 3.3**	**35.8**	**3**
Control	**29.3 ± 2.1**	**-**	**-**

Table 4.1 shows that the combination was produced good % of orthokeratosis it mean it was show anti psoriasis activity.



B. V. + Dithranol



Combination.

5. Evaluation of Depigmentation activity.

Containing 5 group each of 3 animals.

Group 1Combination

Group 2 Hydroquinone

Group 3 Betamethasone valerate

Group 4B.V. + Hydroquinone

Group 5 Control

Table 5.1 Depigmentation activity

Sr.	Treatment	Depigmentation

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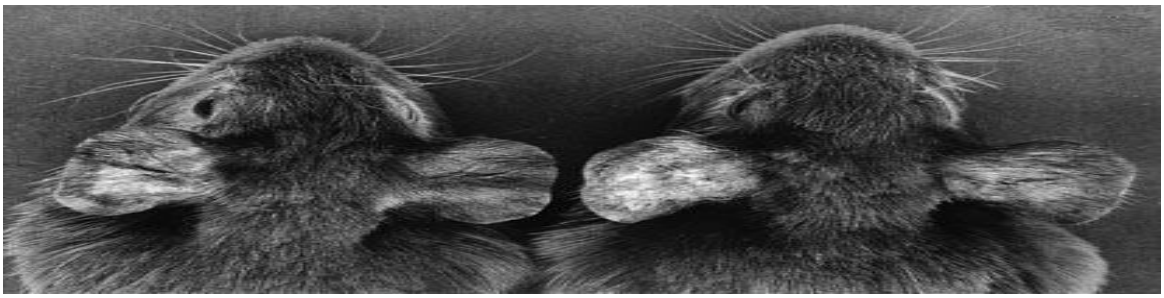
No.		
1	**Combination**	++++
2	**Hydroquinone**	+++
3	**Betamethasone valerate**	++
4	**B.V. + Hydroquinone**	++++
5	**Control (Paraffin ointment)**	±

Depigmentation, Absent 0, Uncertain ± , Week +, Moderate++, Strong +++, Total ++++.

Table 5.1 shows that effect of combination was equivalent to that of B.V.+ Hydroquinone.



Before Treatment After 6 week Treatment.

DISCUSSION

Existing combination of Dithranol & salicylic acid is available in the market in India. (Ointment Ringozone(R)) A stiff dithranol 0.5% ointment shows colour changes, degradation and loss of potency after adverse storage. Varying strength of salicylic acid were added in an attempt to protect the dithranol.[12] The most common corticosteroids used topically for anti-inflammatory activity (*Betamethasone, prednisolone, and derivative, Hydrocortisone.*).[13] Indication of Betamethasone valerate are anti-inflammatory, on eczema, psoriasis.[14] Lignocaine hydrochloride produces local anesthetic effect which will reduces irritation and burning sensation of skin. Also the Betamethasone valerate and Lignocaine HCL combine given in dental anesthetics. The most commonly used treatment for all types of hyperpigmentary disorders is topical hydroquinone.[15] Corticosteroids are also given with hydroquinone in hyperpigmentation during healing step.[16] Salicylic acid is a widely used

keratolytic agent in the treatment of hyperkeratosis conditions such as psoriasis, eczema. Petrolatum containing 10% salicylic acid is a commonly used ointment for this purpose.[17-19]

Study can be explored for further Detail investigation, such as different types of topical formulations, anti eczema, anti dermatophytes, and other models.

CONCLUSION

The present reseach investigation shows that the prepared formulation was found to be compatible, stable, and effective in preclinical study. The prepared formulation can controlled existed preparation side effect.

CONFLICT OF INTERESTS:

The authors declare that there is no conflict ofinterests regarding the publication of this paper.

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