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Acute Dermal Toxicity Studies of Pitika Mardini and Esabdamini in Rodents

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The study was performed to asses the acute dermal toxicity of Pitika Mardini and Esabdamini in male and female Wistar rats. Test substance was applied as such to the shaven skin of group of rats (3/sex) at the dose of 2000 mg/kg body weight. Control group of animals were similarly treated but only with the base. Following dosing the rats were observed for 21 days for mortality and clinical signs of toxicity. Body weight gain was noted weekly. No visible signs of toxicity after treatment such as changes in respiration, circulation autonomic and central nervous system, behavioral pattern were observed in the study. No reaction was observed on the test substance applied area of the skin. similarly, no signs and symptoms were observed in control groups. Gross pathology examination conducted on the animals at the end of 21 days observation period did not reveal any lesion that could be attributable to the toxicity of the test substance. Since no mortality was observed in the study under the condition of this test it is concluded that the dermal LD50 of Esabdamini and Pitikamardini For wistar rats is more than 2000 mg/kg.

Key words – Pitika mardini, Esabdamini, dermal toxicity.

INTRODUCTION

A Word Health Organization survey indicated that about 70–80% of the world's population rely on non-conventional medicine, mainly of herbal source, in their primary healthcare. This is especially the case in developing countries where the cost of consulting a western style doctor and the price of medication are beyond the means of most people. **[1]** Although medicinal plants may produce several biological activities in humans, generally very few are known about their toxicity. Because safety should be the overriding criterion in the selection of medicinal plants for use in healthcare systems **[2]**. On the contrary the traditional system of medicine has enabled those herbal medicines producing acute and obvious signs of toxicity to be well recognized and their use is unavoided **[3]**. Pitika Mardini and Esabdamini formulations are herbal and herbominerals respectively. Extracts are incorporated into suitable bases, but there are chances of contamination which may prove toxic to the individuals or may develop any other complications in future. Hence, present study was taken to investigate the dermal toxicity of Pitika Mardini and Esabdamini possessing antiacne and antieczema activity respectively in rodents.

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MATERIALS AND METHODS

1) Preparation of herbal extracts and herbomineral formulation: -

Pitika Mardini:- Shed dried moderately coarse powders of individual herbal ingredients were mixed together in equal proportions 100 gm of the marc thus obtained was subjected for hot percolation using soxhlet extractor and ethyl alcohol (70%) as a solvent. The extract or was concentrated using rotary evaporator till we get pasty consistency. It was transferred into a Petri dish, kept into desiccator for 24hrs. it was lyophilized for 48 hrs. the dry powders of the extract thus obtained was preserved in polyethylene bags under controlled conditions of temperature and humidity till further use. This extract was coded as EP for Pitika Mardini cleansing cream. The formula is summarized in (Table no. IA IC & ID)

Esabdamini:- Individual minerals and herbal extracts were triturated separately in glass mortar and pestle, sifted those powders through 60 #, 80# and 120# sieves. Fine powders thus obtained were mixed together in equal proportion. Conical blender was used for homogenization of the powder mass. Required quantity of the powder was weighed and incorporated into oily bases to develop Isab damini ointment. It was coded as F1 (Active ingredients). The formula is summarized in (Table no. IB IC & ID)

2) Dermal toxicity studies in Rats: [4,5]

2a) Range finding experiment

Table no. IA Anti-acne: **Pitika mardini (Composition and concentration)**

Sr no.	Botanical name	Common name	Part used & (Wt. in gm)
1	*Rubia cordifolia*(Rubiaceae)	Manjishtha	Roots (20)
2	*Symplocos racemosa* (Symplocaceae)	Lodhra	Bark (20)
3	*Acorus calamus*(Araceae)	Vekhand	Rhizomes (20)
4	*Coriandrum sativum* (Umbelliferae)	Dhania	Fruit (20)
5	*Citrus limonis* (Rutaceae)	Lemon	Fruit (20)

No of animals: For **Pitika mardini** Two (1 male + 1 female) **and Esabdamini** Two (1 male + 1 female)

2b) Main experiment

- No of animals : 24 (12 male + 12 female)
- No of animals/ groups: Six (3males and 3females per group).
- Body weight at the start of experiment:
  Male : 150 – 180 g
  Female : 145 – 170 g

Table no. IB Anti-eczema: **Esabdamini (Composition and concentration)**

Sr no.	Botanical /Chemical name	Common name	Concentration	Formula for ointment (30g)
1	Pb_2O_3	Shendur	0.375 gm-25%	
2	*Cinnamomum camphora,* linn (Lauraceae)	Kapur	0.375 gm-25%	
3	*Uncaria gambier*, Roxb (Rubiaceae)	Kattha / Pale catechu	0.375 gm-25%	F1= 1.5g
4	Litharge (PbO, Lead oxide)	Muddarshing	0.375 gm-25%	

3) Methods for evaluation of Dermato-Toxicity

Pitika mardini and Esabdamini was applied as such to the shaven skin of group of rats (3/sex) at the dose of 2000 mg/kg body weight. Control group of animals were similarly treated but only with the base.

Table no. IC Preparation of Topical Formulation Bases

Cleansing cream base		Ointment base	
Ingredients	**Quantity (g)**	**Ingredients**	**Quantity (g)**
Mineral oil	45	Bees wax	**2**
W.S.P	27	Cetostearyl alcohol	**3**
Bees wax	18	Wool fat	**5**
Lanolin	3.5	White soft paraffin	**90**
PEG	6		
Perfume	0.5		

Table ID Preparation of medicated formulations

Ingredients	Pitika mardini Cleansing cream	Esabdamini Ointment
Polyherbal extract (EP) (% w/w)	**2**	-
F_1 (Active Ingredients) (% w/w)	-	**2**
Cleansing cream base	**q.s.**	-
Ointment base	-	**q.s.**

Note : Above table IC clearly indicate the plane base for application (i.e. without medicines) and Table ID shows the % incorporation of 2 % extract i.e. (2000 mg/kg)

3a) Test procedure

Approximately 10 % of dorsal skin area of each rat was shaved without any abrasion 24 hour before the test. The test substance was held in contact with the exposed skin under a gauze pad upto 24 hour.

Following this the skin was washed with lukewarm water and wiped away with gauze.

3b) Main study

As No mortality was observed in the Range finding study, the study was repeated as a limit tests. In the limit test 3male and 3females were treated with cleansing cream and ointment at dose 2000 mg/kg b.w. Animals in control group was similarly treated with vehicle alone.

All the animals were observed during the entire observation period for any reaction at the application site, change in the fur, eyes mucous membrane and any other overt signs of toxicity including behavioral signs. Body weight determination of each animal was done just prior to administration of test substance 0 day and on days 7 14 and 21 following the administration.

3c)Necroscopic studies- All the animals were necropsied at the end of 21 day observation period. Detailed gross examination was conducted in individual animal of both the groups.

TABLE II mortality data

Group	Total no. of rats treated	Dose (mg/kg b.w.)	Percent mortality (upto 21 days)	
			Male (n=3)	Female (n=3)
I (Base) Control for Pitika mardini	6 (3M+3F)	2000	0	0
II (Base) Control for Esabdamini	6 (3M+3F)	2000	0	0
III Treated with Pitika mardini	6 (3M+3F)	2000	0	0
IV Treated with Esabdamini	6 (3M+3F)	2000	0	0

RESULTS AND DISCUSSIONS

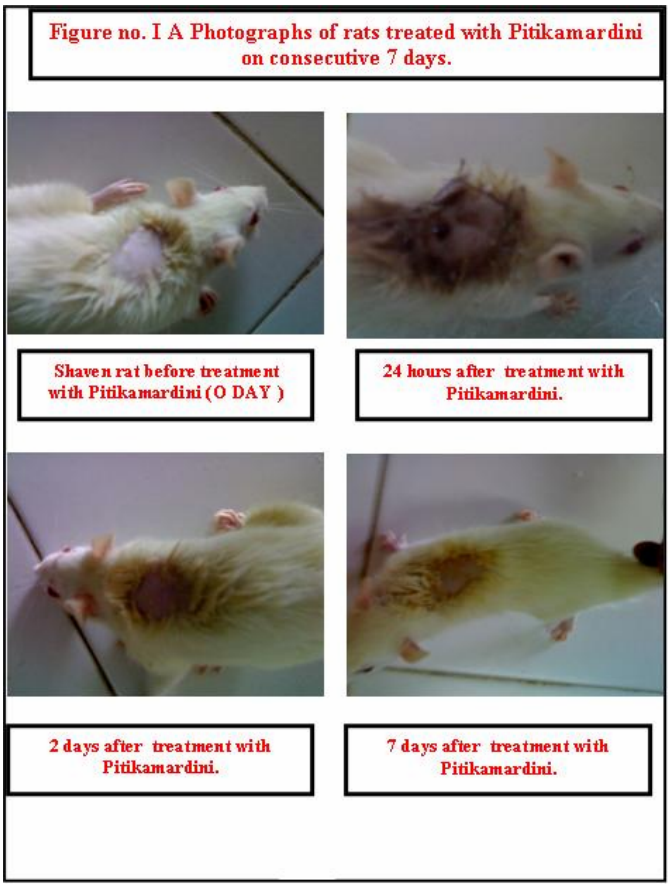
Range finding experiment - In the range finding study 2 animals 1male and 1female were dermal administered with **Pitika mardini and Esabdamini** at the dose of 2000 mg/kg b.w. following the dosing the

TABLE III Weekly body weight data

Group	Dose (mg/kg b.w.)	Body weight (g)			
		Day 0	Day 7	Day 14	Day 21
I (Base) Control for Pitika mardini	2000	160.83 ± 5.388	169.16 ± 4.549	189.83 ± 2.242	213.0 ± 4.243
II (Base) Control for Esabdamini	2000	160.66 ± 3.703	179.33 ± 4.169	194.33 ± 2.486	209.16 ± 4.238
III Treated with Pitika mardini	2000	159.0 ± 2.449	171.66 ± 2.472	181.66 ± 2.789	214.33 ± 5.245
IV Treated with Esabdamini	2000	167.0 ± 3.651	182.50 ± 4.233	195.33 ± 3.323	216.16 ± 4.743

Values are Mean ± S.D.

Figure I Photographs of the exposed skin of rats treated with the formulations IA) Pitika Mardini and IB) Esabdamini from the time of treatment 0th day to 7th day after exposure



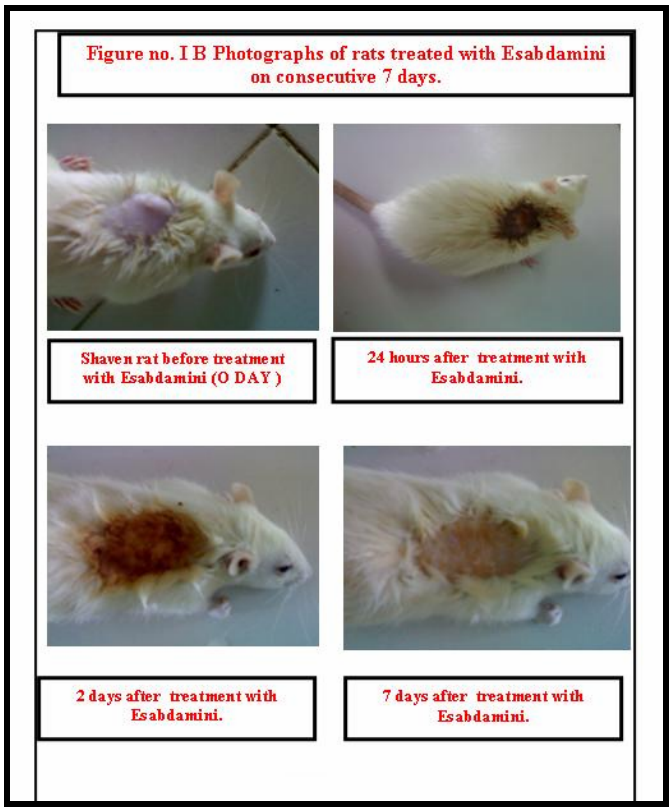


TABLE IV Gross Pathology Data

Group	Lesions in liver, Kidney, Stomach and Lungs.	
	Male (n=3)	Female (n=3)
I (Base) Control for Pitika mardini	NAD	NAD
II (Base) Control for Esabdamini	NAD	NAD
III Treated with Pitika mardini	NAD	NAD
IV Treated with Esabdamini	NAD	NAD

NAD = Nothing Abnormal Detected

animals were observed for five days. No mortality occurred in these animals .

Main test - No mortality was observed in the treated groups and control group of animals (table II)

No visible signs of toxicity after treatment such as changes in respiration, circulation autonomic and central nervous system, behavioral pattern were observed in the study. No reaction was observed on the test substance applied area of the skin similarly, no signs and symptoms were observed in control groups. Table 2 Compared with control animals belonging to the test substance treated group (both sexes) did not show a significant change in body weight gain on days 7, 14 or 21 (Table III)

Photographs of the exposed skin of rats treated with the formulations from the time of treatment to 7th day after exposure are depicted in figure I. The figure shows the effect of the formulations on the exposed skin and change in the skin texture.

Necroscopic examination did not reveal any abnormal lesion in any group. (Table IV)

Since no mortality was observed in the study under the condition of this test it is concluded that the dermal LD50 of Esabdamini and Pitika mardini for wistar rats is more than 2000 mg/kg.

Therefore it may also be concluded that both the formulation are safe for usage in the management of acne and eczema.

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