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# Role of hepatoprotective drugs in the management of skin disorders with special reference to *Kitibha* (psoriasis): A case study

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## Abstract

**Psoriasis is fundamentally an inflammatory skin condition with reactive abnormal epidermal differentiation and hyper-proliferation affecting 2-3% of world's population. Pathophysiology of the disease includes mainly the activation and migration of T cells to the dermis triggering the release of cytokines (tumor necrosis factor-alpha TNF-alpha, in particular) which lead to the inflammation and the rapid production of skin cells. Considering the morbidity in psoriasis & loss of effectiveness of present treatment, psoriasis is screened in light of *Kitibha* disease (*Kushtha*) as mentioned by *Acharya Charaka*. The etiological factors, symptomatology, and complications of *Kitibha* compared with that of psoriasis, grand similarity was revealed. A preliminary randomized single blinded controlled clinical trial of drugs in 46 cases of psoriasis was conducted, to prove the practical approach of management of psoriasis. For this clinical study divided into following groups viz. Group A (10 cases were given 3 gm *Daruharidra* per day in 3 divided doses), group B (10 cases were provided 3 gm *Kalmeg* per day in 3 divided doses) and Group C (10 cases were given combination of both i.e.1g each per day in 3 divided doses), *Group D (*Placebo control group consisting of 8 patients were given wheat flour as 6 capsules in 3 divided doses) and *Group E (*Standard Controlled Group, having 8 patients who were administered with *Methotrexate* 7.5 mg once a week). The trial drugs were given for a period of three months to each patient. Controlled group was more effective (75%) as compared to combine group but reoccurrence was frequent in controlled group. Combined Group (A+ B) reveal 51% and *Daruharidra* reveals (40%) relief. When *Daruharidra* and *Kalmeg* are given alone give better result but when adding together has shown additive effect similar to standard control group Methotrexate.**

**Key words:** ***Kitibha, Psoriasis, Hepatoprotective Drugs.***

## Introduction

Psoriasis is a painful, disfiguring and disabling disease for which there is no cure and with great negative impact on patient's quality of life (QoL) (Aromdee, 2012). The reported prevalence of psoriasis in worldwide ranges between 0.09% and 11.4%, making psoriasis a serious global problem with at least 100 million individuals affected worldwide. Psoriasis causes great physical, emotional and social burden. Psoriasis is a disease in which there occurs spontaneous remissions, relapse and seasonal variations. Psoriasis is seen all over worldwide. In most developed countries, prevalence is seen in between 1.5 and 5% (Sharma, 2009). Prevalence of psoriasis is increasing day by day. Existing treatment is frequently inadequate (decreased effectiveness on prolong use along with some major side effect like marrow depression). Measures are required to prevent the development of psoriasis and to improve treatment and control of psoriasis in the community. The disease psoriasis and its symptoms as a whole are not present as a single entity in *Ayurveda* (Roy *et al.,* 2010). On the basis of strong similarity between etiological factor, symptom, and *Doshika* involvement in the etiopathology and complications of psoriasis can be correlated with *Kitibha* (Chao and Lin, 2010). Liver is responsible for most of the enzymatic activities & any disturbance in its activities leads to *Agnimandhya*. Unhealthy liver plays an active role in the development and recurrence of psoriasis (Stern *et al.,* 2004). By reducing the amount of toxins in liver, relief from skin diseases may occur. Sedentary life style, improper food habits, external factors causes *Agnimandhya* (*Rasadusti*) resulting in *Rasa Pradoshaja Vikara (Kustha*). Thus to break the pathogenesis, there is need of drugs that work on liver & improves digestion & enzymatic activities. Hence for purpose of *Deepan-Pachana* hepatoprotective (trial) drugs are taken so that basic root cause (*Agnimandya*) treated & patient got

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relief from symptoms. The trial drugs were also described as *Kushthaghana, Vranshodhaka* and for loss of sensation of skin. The trial drugs were described as hepato-protective drugs. Further these also alleviate *Agnimandhya* & act as *Pita Sarak* .With this background, it is planned to evaluate the efficacy of Hepatoprotective drugs (*Daruhridra*, *Kalmeg*) in the management of psoriasis (Danielsen *et al.,* 2004; Ronald and Nussbaum, 2015).

## Materials and Methods

The patients for the present clinical study were selected randomly from dermatology and skin Outdoor Patient Department (OPD) of *Kayachikitsa*, S S Hospital, and B.H.U. Varanasi irrespective of gender, caste, religion, occupation, etc. All the patients were screened through various relevant investigations for psoriasis. The cases were recorded and registered with the help of special proforma prepared for purposes.

**Inclusion Criteria:** The patient having localized and generalized Guttate and Palmo-planter psoriasis were included in this present study. The patients between age group in between 7 to 80 years were taken and patients having hereditary predilection were also included in the study.

**Exclusion Criteria:** Psoriatic arthropathy, Psoriatic Erythroderma, Cardiac disease, Renal disease, Endocrine Disorders and the patient having any other associated disease.

**Investigations:** Routine hematological investigations – Hemoglobin%, Total Leukocyte Count (TLC), Differential Leukocyte Count (DLC), Erythrocyte Sedimentation Rate (ESR), Blood sugar, Blood urea and Serum creatinine, ASO Titre, LFT

Total 71 patients were registered for the trial, out of which 46 were followed up to the last follow up and divided into three groups for this clinical study.

**Groups of treatment:** The patients were randomly categorized into the following three groups.

**Trial drugs**

**Group A (*Daruharidra*)**

In this group, a total of 10 patients completed the course of treatment.

**Group B (*Kalmeg*)**

In this group, a total of 10 patients completed the course of treatment.

**Group C (*Daruharidra* and *Kalmeg*)**

In this group, a total of 10 patients completed the course of treatment.

**Group D (Placebo group)**

In this group, a total of 8 patients completed the treatment.

**Group E (Controlled Group (Methotraxate)**

In this group, a total of 8 patients completed treatment.

**Schedule for trial drugs:** As the trial drugs extract of *Daruharidra* and *Kalmeg* are taken as herbal preparation. These were used in the dosage of 1000mg (2 capsules) thrice daily with lukewarm water and thus a total of 3000 mg (3 gm.) were given per day (Parisi *et al.,* 2013).

**Duration of treatment**: The trial drugs were given for a period of three months to each patient. The patients were followed up every month end the drugs were continued as a part of therapy further after trial period with instruction to follows do's & don'ts. No allopathic or any other drugs for psoriasis were taken during trial (Devaraj *et al.,* 2010; Fuji *et al.,* 2012).

**Parameters of Assessment**

Reports of patient's own observation,
General assessment of investigator,
Photograph taken at regular intervals,
Adverse effects (if any).

**Criteria for Diagnosis of Kitibha Vis A Vis Psoriasis:** Sharply demarcated lesions with clear cut margin, Surface consists of non–coherent scales, beneath the scale homogenous erythema, Austpitz sign positive, Positive candle grease sign or onion peeling sign.

**Scoring:** To assess difference before and after treatment, the four main anatomic sites were assessed: head (h), upper extremities (u), trunk (t) and lower extremities (l) roughly corresponding to 10, 20, 30 and 40 of body surface area (BSA) respectively. The PASI (psoriasis area and severity index) score is adopted for evaluation of psoriasis

**Assessment on the basis of improvement**

| | |
|---|---|
| Significant improvement | 71-80% |
| Moderate improvement | 61-70% |
| Mild improvement | 31% - 60% |
| No improvement | 0- 30 % |

## Results and Discussions

However, majority of the patients (30.43%) were between 21-30 years of age. 26.09% patients were

**Table 1. Final assessment of result in different groups (n=46)**

| | Significant improvement(60-80% or above) | Moderate improvement (30-60%) | Mild improvement upto 30% | No improvement 0% |
|---|---|---|---|---|
| Group A | 40% | 20% | 20% | 20% |
| Group B | 0% | 20% | 40% | 30% |
| Group A+ B | 50% | 30% | 10% | 10% |
| Controlled group | 75% | 12.5% | 12.5% | 0% |

**Table 2. PASI score mean +- S. D.**

| GROUPS | B. T. | A.T.1/F U 1 | AT 2/FU2 | AT3/FU3 | MEAN DIFFER(BT–AT) | Significant 't' value within groups |
|---|---|---|---|---|---|---|
| A(n=10) | 20.56<br>14.69 | 20<br>14.44 | 19.73<br>13.83 | 19.28<br>13.91 | 1.28<br>1.40 | t =2.90<br>p<0.02 |
| B [ n=10] | 19.94<br>10.54 | 19.91<br>10.23 | 19.97<br>10.14 | 19.80<br>10.06 | 0.49<br>0.94 | t =1.68<br>p>0.05 |
| A +B[N=10] | 16.14<br>14.55 | 14.19<br>12.17 | 13.06<br>11.74 | 9.57<br>9.06 | 6.64<br>5.62 | t =3.75<br>p<0.01 |
| Placebo[n=8] | 16.03<br>12.23 | 20.02<br>16.74 | 20.50<br>15.75 | 20.45<br>15.32 | - 0.31<br>0.92 | t= 0.96<br>p>0.05 |
| Controlled[n=8] | 23.50<br>13.70 | 20.95<br>12.10 | 16.98<br>11.75 | 14.85<br>11.06 | 15.08<br>8.85 | t=5.44<br>p<0.001 |

**Table 3. PASI SCORE MEAN +- S.D.**

| GROUPS | B.T. | A.T.1/FU1 | AT2/FU 2 | AT3/FU 3 | Mean diff.(BT-AT) | Paired 'T'Value | Unpaired't' value |
|---|---|---|---|---|---|---|---|
| A{n=10} | 20.56<br>14.96 | 20.00<br>14.44 | 19.73<br>13.83 | 19.28<br>13.91 | 1.28<br>1.40 | t = 2.90<br>p<0.02 | t = 2.78<br>p<0.02 |
| Placebo {n=8} | 16.03<br>12.23 | 12.02<br>16.74 | 20.50<br>15.75 | 20.45<br>15.32 | - 0.31<br>0.92 | t=0.96<br>p>0.05 | |

**Table 4. PASI SCORE mean =-S.D.**

| Groups | B.T. | A.T.1/ FU1 | AT2/FU 2 | A.T.3/FU3 | Mean Diff.(B.T.-A.T.) | Paired 't' value | Unpaired 'T' Value |
|---|---|---|---|---|---|---|---|
| B[n=10] | 19.94<br>10.59 | 19.91<br>10.23 | 19.97<br>10.14 | 19.80<br>10.60 | 0.49<br>0.94 | t = 1.68<br>p>0.05 | t=2.15<br>p<0.05 |
| Placebo[n=8] | 16.03<br>12.23 | 20.02<br>16.74 | 20.50<br>15.75 | 20.45<br>15.32 | - 0.31<br>0.92 | t =0.96<br>p>0.05 | |

**Table 5. PASI SCORE MEAN ± SD (comparison)**

| Group | B.T. | A.T1/FU1 | A.T2/FU2 | AT3/FU3 | Mean diff BT-AT | Paired t value | Unpaired t value |
|---|---|---|---|---|---|---|---|
| Controlled (n=8) | 23.40<br>13.70 | 20.95<br>12.10 | 16.98<br>11.75 | 14.85<br>11.06 | 15.08<br>8.85 | T= 5.44<br>P<0.001 | T = 2.58<br>P 0.02 |
| A+B N=10 | 16.14<br>14.55 | 14.19<br>12.17 | 13.09<br>11.74 | 9.57<br>9.06 | 6.64<br>5.62 | T=3.75<br>P<0.01 | |

A mean change 15.08+- 8.85(t=5.44, p<0.0o1) & 6.64+-5.62 (t =3.75, p<0.01) were significant in both controlled and combined (A+B) group.

An inter group comparison showed between controlled group & combined (A+B) group statistically significant (t =2.58, p=0.02) .

**Table 6. One way ANOVA (STUDENT - NEWMAN KEULS MULTIPLE COMPARISON TEST**

| | Mean rank difference | Q | P value | Significance |
|---|---|---|---|---|
| *Daruhridra vs* Methotraxate | -1.325 | 3.503 | <0.05 | S |
| *Kalmeg vs* Methotraxate | - 1.725 | 4.560 | <0.05 | S |
| Combined *vs* Methotraxate | - 1.025 | 2.710 | >0.05 | NS |
| Placebo *vs* Methotraxate | - 2.500 | 6.270 | <0.001 | HS |
| *Kalmeg vs* Combined | -0.7000 | 1.963 | >0.05 | IS |
| Combined *vs Daruhridra* | -0.3000 | - | >0.05 | IS |
| *Kalmegh vs Daruhridra* | -0.4000 | - | >0.05 | IS |
| Placebo *vs Daruhridra* | - 1.175 | 3.106 | > 0.05 | IS |
| Placebo *vs Kalmeg* | -0.7750 | | > 0.05 | IS |
| Placebo *vs* Combined | - 1.475 | 3.899 | <0.05 | S |

**Comparative effect of different indigenous compounds on PASI score of psoriasis by one way ANOVA Test**

having *Vata–Pitta Deha Prakriti*, 13.04% patients were having *Vata–kaphaja Deha Prakriti* and 60.87% patients were having *Pitta- Kaphaja Deha Prakriti.* Majority of the patients (69.55 %) were males. Patients reported of lower middle socioeconomic status was 36.96% & 34.78 % were of lower group. According to occupation, students reported were 26.08%, house wives 17.39% & labors were 17.39%. Dietary history reveals 78.26% patients were Vegetarian (Gibbs, 1996). Hereditary relationship found in 21.73%. Rural patient were 67.39%. Cases of good hygiene were 28.27%, 58.69% were having moderate type of hygiene & 13.06% were of poor hygiene. Non addicted (52.17%) are equally prone to psoriasis in comparison of addicted persons of different type. 50% patient were suffering from disease for more than 3 years. Stress factor was observed in 58.70%. Maximum (39.13%) incidences reported in winter season, 17.39% in *Hemant* & in *Grishm* 13.04%. Patients in this study reported clinical symptoms like Erythema 100 %, Induration 100%, Scaling 100%, Itching 73.91%, Burning sensation 39.13%, Fear of spread of lesion were in 39.13%. Plaque type psoriatic patients reported were 21.74%, 13.04% were of Guttate type, 34.04% were of Palmoplanter type, 8 .70% were of Numera type & others were 21.74%. Comparing the effect of trial drugs on psoriasis and other associated complaints, it was seen that effect in combined group was better (Lin *et al.,* 2009). Maximum effects were seen in controlled group with frequent reoccurrence of symptoms. Combined group & *Daruhridra* showed better results in the overall effect of drugs. The effect of

combined group was more than that of group A [Tables 1-5].

On applying one-way ANOVA test, there is seen statistically no significant difference between group A (*Daruhridra*) and group D (placebo) but on the basis percentage relief group A (40%) is better than placebo group (4.5%). There is no statistical significance found between group B (*Kalmegh*) and Placebo (group D) but on percentage relief group B (29%) is better than placebo group (4.5%). Though individual effect of Group A (*Daruhridra*) and Group B *(Kalmegh*) when compared with Placebo has shown insignificant result but on percentage basis of improvement they were better than Placebo. Combine group (A+B) (51%) has shown statistical significant difference with placebo (4.5%) with P<0.05. There is existence of statistical significance found between Group C (combined group) with Group E (methotraxate) which state that both the group have comparable effect. Statistically highly significant difference found between placebo group and methotraxate (group E) with P <0.001 (Hsieh *et al.,* 2007).

**Discussion on usage of hepatoprotective drugs as treatment modality in psoriasis:**

To support the concepts of use of hepatoprotective drugs in psoriasis, various studies are taken into considerations which are further:

Liver is responsible for most of the enzymatic activities & any disturbance in its activities leads to *Agnimandhya* (*Rasadusti*) resulting in *Rasa Pradoshaja Vikara (Kustha*). Multiple hospital-

based observational studies suggest patients with psoriasis are 1.5-fold to threefold more likely to have NAFLD (Non-Alcoholic Fatty Liver Disease). Psoriasis patients with NAFLD (PV-NAFLD) were more likely to have metabolic syndrome, higher C-reactive protein, and greater psoriasis area and severity index (PASI) scores than psoriasis patients without NAFLD. A subgroup of this PV-NAFLD group had elevated interleukin-6 (IL-6) and lower adiponectin levels. Both psoriasis and NAFLD are associated with metabolic conditions, such as metabolic syndrome and obesity. Thus it has been unclear whether psoriasis itself is independently associated with NAFLD By the reducing the toxins from liver, relief from skin diseases may occur.

Probable Mode of Action of trial drugs can be understood in the following ways: (1) by anti inflammatory mechanism, (2) by liver activity improvement and (3) by anti hyperproliferation activity. Because of *Tikta Ras, Laghu, Ruksha Guna, Ushna Virya, Katu Vipaka* of *Daruhridra* (Berberis aristata), it is *Yakrit Uttajaka* (liver stimulant) & *Pitta Sarak*. In a study, Berberine (active compound found in Berberis aristata) possesses hepatoprotective effects & effect as both preventive and curative. Serum ALT and AST activities significantly decreased in a dose-dependent manner in both pre-treatment and post-treatment groups with berberine. It increased the tissue superoxide dismutase (SOD) activity in liver & lowers the damage of liver. Histological examination showed lowered liver damage in berberine-treated groups'. Berberine inhibited inflammation and low-density lipoprotein (LDL) oxidation. (ALT) and aspartate aminotransferase (AST) levels were ameliorated after berberine treatment. Anti-inflammatory mechanism of berberine, an isoquinoline alkaloid, is mediated through cyclooxygenase-2 ((COX-2) plays a key role in prostaglandins (PGs) synthesis, which is elevated in inflammation) regulation. This berberine induced effect occurred rapidly (3 h) as a result of reduced COX-2 protein, but not enzyme activity. Berberine may protect LDL oxidation and prevent oxLDL-induced cellular dysfunction.

Neutrophils are more likely to adhere to endothelium during inflammation and, subsequently, infiltrate into site(s) of tissue injury where they release hydrolytic enzymes and large amounts of ROS to induce tissue damage. Uncontrolled production of these radicals by phagocytes could lead to tissue injury during inflammation. For example, it is known that exaggeratory ROS (reactive oxygen species), production by neutrophils plays an important pathological factor for many inflammatory disorders, such as in the induction of ischemic and reperfused injury. Because of Antiadhesive and anti transmigration effect of drug, ANDRO (andrographolide) may be useful for the improvement of neutrophil infiltration & having anti inflammatory effect (Kimball *et al.,* 2005).

In vitro studies on *A. paniculata* have shown the presence of many bioactive constituents having pharmacological as well as medicinal properties which include its activities as anti-inflammatory[i], antioxidant, antiproliferative effect hepato-protective Studies provide the evidence of antioxidant activities of *A. paniculata.*

## Conclusion

On the basis of the above result we can say that when *Daruhridra* and *Kalmeg* are given alone give better result but when add together has show additive effect similar to standard control group Methotraxate. *Daruhridra* may be the treatment of choice in conditions where psoriasis is associated with itching especially when combined with *Kalmeg*. Placebo and controlled group were statistically insignificant in itching symptoms. Trial drugs used in this research may be used as a good treatment modality for the management of the psoriasis & will be proving as a boon for sufferers & pave the path to researchers by providing a culture of study. Other varieties of hepatoprotective drugs may be tried for disease like psoriasis & others.

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