



Review Article

**INCORPORATING *DUSHIVISHAJANYA ROGAS* TO AUTOIMMUNE SKIN DISORDERS-
BREAKING THE CELL MEMBRANE IMPERMEABILITY- A CONCEPTUAL STUDY**

Aswani Krishnan K^{1*}, Seemaja G²

*1PG Scholar, ²Associate Professor, Department of Agadatantra, Government Ayurveda Medical College, Thiruvananthapuram, Kerala, India.

Article info

Article History:

Received: 11-01-2026

Accepted: 18-02-2026

Published: 26-03-2026

KEYWORDS:

Dushi visha,
Sookshma, *Leena visha*,
Toxins.

ABSTRACT

Vagbhata described *Dushi visha* as a type of *Visha*, which do not have the combination of all gunas to create immediate toxicity in the body. For instance, it is the *Visha* which is not that *Vyavayi*, *Vikashi* and *Sookshma*, so it cannot spread quickly. Instead, they create a '*Leena visha*' *Avastha* (dormant stage) in the body, lodging somewhere in the body because the gunas are not potent enough to destroy the *Ojas* immediately, but can affect it eventually. These toxins reside in the body, where they have affinity, and get covered by *Kapha* over the period. They can reside anywhere in the body where their affinity matches (owing to *Samanya vishesha sidhanta*). They can reside in *Amasaya* causing *Kaphavata rogas* and in *Pakvasaya* causing *Vatapitha rogas*. They can reside in *Dhatus*, from *Rasa*, *Rakta* to *Sukra*. Even in the *Leena Avastha*, they can cause disturbances in the body mentioned as *Dushi visha poorvarupa* by *Sushruta Acharya* like more of sleep, feeling of heaviness of body, more of yawning, looseness of joints, tingling or diffuse pain in the body. The concept '*Kaphavrtham Varshagananubhanthi*' (covered by *Kapha*, it remains in the body), can be correlated with toxins being depositing on the protein receptors of the cell membrane, causing protein receptor modification, and breaking its permeability gradually. Toxins enter the cell wall to nucleus and DNA, and cause genetic mutation. Ultimately, the cell loses its structure and function. The function that cell has been doing will be abruptly and this gives rise to many diseases especially autoimmune diseases, because when the cell loses its self-intolerance, it can't distinguish between self and outside. The study focuses on incorporating *Dushivisha* with autoimmune skin diseases by comparing both of their pathogenesis.

INTRODUCTION

In the last decades, increasing evidence is accumulating for a steady rise in the frequency of autoimmune diseases (AD)^[1]. Their relationship to socioeconomic status, their rapid increase in developed countries and observations in selected migrant populations, indicate some form of environmental impact, rather than long-term genetic influences which are driving these recent evolutionary processes. Among many others, three major environmental factors, strongly related to

socioeconomical status are suspected to drive these phenomena: infections, ecology and nutrition^[1,2,3,4,5]. The diagnosis and treatment for autoimmune diseases especially of skin is challenging in every stream of medicine, also there is no enough diagnostic tools to know it earlier. Autoimmune skin diseases are more challenging due to their chronic and relapsing nature. Most of the treatments for autoimmune diseases in modern medicine focusses on corticosteroids, immunosuppressants and anti-inflammatory drugs which is not good for the body in the long run. Also, skin diseases have got great emotional and psychological impact that cannot be neglected.

The age-old wisdom of Ayurveda has one stream of medicine as *Agadatantra* which focuses on the anti-toxic study. Autoimmune diseases' pathology has similarity with the pathology of *Dushivisha* in *Agadatantra*. Detailed prodromal symptoms,

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Quick Response Code	
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manifested symptoms along with their treatment are explained in the context of *Dushivisha*. The study focusses on incorporating *Dushivisha janya rogas* to autoimmune skin disorders at genetic level.

The barrier which protects the genes from getting triggered is 'cell membrane', because of its impermeability, they allow only the selected particles in and out of the cell. But due to several environmental stress, the cell membrane structure and function is affected making it permeable to everything, which gives the chance for a mutation.

Dushivisha and autoimmune diseases will be discussed in the epigenetic level and their common features will be further studied to help in the Ayurvedic management of autoimmune diseases.

AIMS AND OBJECTIVES

To incorporate *Dushivishajanya rogas* to autoimmune skin disorders, by studying at genetic level.

MATERIALS AND METHODS

The pathogenesis of both *Dushivisha* and autoimmune skin diseases are read, analysed and compared.

Review of Literature

Dushi Visha and *Visha Guna*

Visha gunas^[5] are:

1. **Ruksha:** It causes *Vata kopa*, it destroys body like when fibers are destroyed, whole cloth is destroyed.
2. **Ushna:** it causes *Pitharaktha kopa*.
3. **Theekshna:** destroys *Marma*, causes *Mano dushti* and causes *Pitharakthakopa*.
4. **Sookshma:** due to this *Guna*, *Visha* can enter all body organs and can cause diseases.
5. **Aashu:** this means the *Visha* quickly mixes with *Annarasa* and spreads quickly.
6. **Vyavayi:** quickly spreads to all parts of the body.
7. **Vikashi:** reduces function of *Dosha*, *Dhatu* and *mala*, destroys *Marma*.
8. **Visadam:** spreads throughout body without getting adhered.
9. **Laghu:** difficult to expel from the body due to its minute nature, and also difficult to treat.^[6]
10. **Apaki/vishamapaki:** unable to digest. Harms body for a long time, as it remains in the body for a long time.
11. **Avyaktharasa:** *Visha* is a mixture of *Rasas*, so it has multiple *Dosa* vitiation, especially *Kapha*.^[5]

It is because of the combination of these *Gunas*, the *Visha* is strong enough to destruct *Ojas* from the body as the *Ojas* has completely opposite *Gunas* of *Visha*. With these *Gunas* only, the *Visha* can destroy the person taken it immediately (*Sadyo harathi jeevitham*).^[5]

Vagbhata described *Dushi visha* as a type of *Visha*, which do not have the combination of all *gunas* to create immediate toxicity in the body. For instance, it is the *Visha* which is not that *Vyavayi*, *Vikashi* and *Sookshma* and it cannot spread quickly. Instead, they create a '*Leena visha*' *Avastha* in the body, lodging somewhere in the body because the *gunas* are not potent enough to destroy the *Ojas* immediately. Acharya describes several factors in which the potency of *Visha* is reduced.

1. **Jeernam** (very old)

With time, the particle loses their *Tikshanata*, *Rukshatha* and *Ushnatha*, they are being exposed to several seasons which include heat, cold, humid etc. this may decay the original potency of the drug. Also, the *Laghutwa* of the drug may be lost with the accumulation of exogenic factors over the particle.

2. **Vishagnoushadibhirhatham** (inactivated by anti-poisonous drugs)

The person immediately takes *Vishagna oushada*, which can destroy *Visha* properties to a large extent, but not strong enough to completely expels it from the body, this can lead the *Visha* persists in the body in *Leena* form without causing immediate effects. Most of its *gunas* are overcome by the *Vishagna agada*.

3. **Davagnivataatapashoshitham** (evaporated by forest fire, wind and sun)

The drugs are being partially destroyed by the external factors. The part carrying most potent *Visha* will be destroyed.

4. **Swabhavatho** (by nature)

By nature, the particle does not have all the *gunas* to create an immediate toxicity. But can cause a little troubles and reside in the body as *Leena visha*.^[5]

***Dushi Visha* Getting Active to Form Skin Diseases**

These toxins reside in the body, where they have affinity, and get covered by *Kapha* for a long time. They can reside anywhere in the body where their affinity matches (owing to *Samanya vishesha sidhanta*). They can reside in *Amasaya* causing *Kaphavata rogas* and in *Pakvasaya* causing *Vatapitha rogas*. They can reside in *Dhatu*, from *Rasa*, *Rakta* to *Sukra*. Even in the *Leena avastha*, they can cause disturbances in the body mentioned as *Dushi visha poorvarupa* by *Sushrutha Acharya* like more of sleep, feeling of heaviness of body, more of yawning, looseness of joints, tingling or diffuse pain in the body. But when favorable period arises, there is a breakage of *Kapha avarana* and *Visha* dispels to *Rasa raktadi dhatus*.^[6] The aggravating factors include.

1. **Prakvata** (environmental stress)
2. **Ajeerna** (digestive issues)
3. **Seethabra** (environmental stress)
4. **Divaswapna** (disruption in circadian rhythm)
5. **Ahitasana** (dietic irregularities)

The *Tridosha kopa* caused due to these reasons destroy the equilibrium of *Dosas*, breaking the *Kapha Avarana*, causing *Visha* to break into the *Rasa, Rakthadi dhatus* causing disorders which includes indigestion of food, loss of taste, 'appearance of round patches and rashes on the skin', delusion, loss of tissues, swelling of feet, hands and face, ascites, vomiting and diarrhea.

When greatly increased it produces discoloration of the body, fainting, irregular fever and profound thirst. Some kinds produce insanity; some produce flatulence; some causes decrease of semen; yet others produce '*Kushta* or skin disease'. The toxin causes a wide spectrum of somatic and psychosomatic diseases according to the affinity of poison, character of the particle, character of the exacerbating factor and immunity of the individual.

Since it becomes aggravated often by habitat, season, food and day sleep, and since it vitiates dhatus, it is called *Dushi visha*.

Dushi Visha Chikitsa

The person should be given '*Suswedana*'- mild '*Sneha*' intake and sudation therapy in a large amount, to detach it from the *Leenavastha* and bring it to *Koshta*. Then it is expelled through upper and lower GIT. Then, in the *Shoditha avastha* (after purification), he is made to take '*Dushivishari agada*' which has the abundance of *Vishagna* (antitoxic) drugs and *Amapachana* drugs which will neutralize the remaining *Visha*. The person should follow the *Pathya in Ahara* (food) and *Vihara* (regimen) and be careful in every habitat and season since, there is a chance of recurrence of *Dushi visha* always. For the one who is weak and who indulge in unsuitable activities and food, the disease becomes '*Asadhya*'^[5].

For *Dushivisha*, more than cure, prevention is necessary. In modern world, every fruit and vegetable are sprayed with preservatives and chemicals to prevent decaying. Gradually, these enter into the food chain and reaches human body. So, prevention can be done by following the *Rtucharya* and *Dinacharya* as explained in different Ayurveda Classics. Doing *Sodhana* of body appropriately as per the season and following *Pathya* in food and regimen can protect us from *Dushivisha* to a large extent.

Cell Membrane- Structure

Cell membrane or plasma membrane or plasmalemma is the outer protective wall of the cell. It helps in maintaining the shape and size of the cell. Any exchange to and from the cell happens only through the cell membrane. Cell membrane is thin and pliable.

It has 10nm thickness. Its main constituents are lipids (40%), proteins (55%) and carbohydrates (5%).

Lipids are arranged as bilayer. It consists of two kinds of lipids- phospholipid and cholesterol. A phospholipid molecule consists of phosphate head (hydrophilic) and lipid tail (hydrophobic). Thus, phosphate groups come in side contact with water and lipid groups come in opposite side forming a bilayer, without creating any strong bonds with each other. These molecules are freely moving and are in liquid state, commonly known as the fluid mosaic model of the membrane. Cholesterol lipids are dissolved in the lipid bilayer. At modest level, it decreases the fluidity, at high concentration it increases the fluidity thus reducing the membrane rigidity. This lipid bilayer is semi permeable allowing only limited constituents inside and out. Proteins and carbohydrates are attached to this lipid bilayer.

Cell Membrane-Permeability

Factors regulating which molecule to enter or exit the membrane

1. Molecule size

Small molecules find much easier to pass the gap between lipid bilayer

2. Concentration gradient

By diffusion molecules move from higher concentration to lower concentration to attain a dynamic equilibrium.

3. Polarity of molecule

The molecules should have to pass the non-polar hydrophobic area.

Fate of toxin accumulation in cell membrane

The toxins over cell membrane are arrived from both outside and inside body.

Free radical and lipid peroxidation

The toxins create free radicals, which has free electrons causing lipid peroxidation, bombarding the cell membrane bilayer and polarity. The phosphate head can become dysfunctional and inflamed.

Attachment of toxins

Toxins get lodged in cell membrane in lipids, phosphates, proteins or carbohydrates.

Protein Receptor modifier

It can happen due to lipid peroxidation or attachment of toxins which have affinity to proteins

Cell functions get affected

The functions done by the particular cell become less efficient, which leads to diseases and chronic illness.

Aggravating factors

1. Lack of antioxidants in the body or its reduction.
2. Inefficient lipid- phosphate turn over system.
3. Exhausted oxidation-reduction system due to overload.

4. No proper elimination and nourishment.
5. Emotional stress or trauma.
6. Discrepancy in circadian rhythm.
7. Gut microbiome changes.
8. Environmental stress- pollution, chemicals.
9. Ultraviolet radiation.

Environmental stress and autoimmune diseases-epigenetics

Self-tolerance is required for normal immune function, and lack of it causes autoimmunity. Recent evidence shows that environmentally-induced epigenetic changes, and in particular altered patterns of DNA methylation, contribute to the environment-host interaction in some forms of autoimmunity. A failure to maintain epigenetic homeostasis, due to environmental influences, can lead to aberrant gene expression in specific cells which cause loss of tolerance, and the modified cells then contribute to the development of autoimmunity in genetically predisposed individuals.^[7] The skin is exposed to vast range of environmental factors, including UV radiation, and is prone to the development of autoimmune conditions such as atopic dermatitis, psoriasis and some forms of vitiligo, based on environmental and genetic influences.^[7] The response of demethylated CD4+ cells to self-class II MHC molecules demonstrates that normal, antigen reactive T cells can be modified by external agents to become autoreactive which can potentially contribute to an autoimmune disease.

Psoriasis is a chronic inflammatory skin disorder featured by excessive proliferation of keratinocytes. Onset of psoriasis is connected to genetic, immune and environmental factors. The environment can interact with the genome through epigenetic modifications, including DNA methylation, and this modification is involved in the pathogenesis of psoriasis.^[8] A possible pathogenesis hypothesis about psoriasis suggests that abnormal activation and migration of T-cells into the skin and eventual aggregation of inflammatory cells, followed by psoriatic-plaque development, mediated by CD4+ and CD8+ T-cells.^[9]

Immune-mediated mechanisms have been recognized in lichen planus since environmental factors can trigger the disease in genetically susceptible individuals. Host immune response dysregulation, as terminally differentiated and virus-specific CD8+ T lymphocytes have been found in the LP lesions.^[10]

The prevalence of Atopic Dermatitis continues to increase in industrial countries, risk factors for the disease.^[11] These studies suggest other non-genetic contributors to AD pathogenesis that may include environmental interactions and epigenetic changes.^[12] A more current study that investigated

additional CD4+ T cell subsets and CD8+ T cells identified DNA methylation changes that were cell type-specific in Atopic Dermatitis patients.^[13]

Systemic lupus erythematosus is a multisystem autoimmune disease which is characterized by immune complex accumulation in blood vessels and connective tissue.^[14] Studies shows that the etiological factors of lupus include the genetic susceptibility, environmental factors and epigenetics. Lupus patients showed global T-cell hypomethylation in studies.^[15]

Studies show that compared with healthy individuals, methylation levels of peripheral blood mononuclear cells (PBMCs) exhibited global hypermethylation in vitiligo patients.^[16]

DISCUSSION

In modern era, *Dooshi visha* can be related to anything which enters our body and gradually becomes poison. From the polluted air we exhale daily to the apple we eat which is sprayed by pesticides are *Dooshi visha*. Even the stress we feel daily are generating stress hormones which create a huge oxidative stress in the body. In this digital era, people's sleep rhythm is totally disturbed. Some people have no choice than to take the night shift which creates a huge discrepancy in melatonin-cortisol level. These are natural antioxidants of the body, which are all imbalanced. Due to several such reasons, mass of free radicals is generated in the body.

Cell membrane of a cell can be considered as the protective brain of a cell. It controls what to enter and exit a cell. The toxins regenerated, according to Ayurveda is *Sookshma*, *Laghu* and *Apaki*, it will not be destroyed nor eliminated out of the body. This makes these toxins to remain in the body as "*Leena visha*". It is covered by *kapha* for a long time. In parallel to this, the toxins get attached to the cell membrane-in lipids, phosphates or proteins according to its affinity. Gradually, these toxins create problems in the cell membrane when the favourable conditions arise.

As in Ayurveda, as favourable conditions arise, this become *Dushivisha*, here due to the factors like lack of antioxidants in the body or its reduction, inefficient lipid- phosphate turn over system, exhausted oxidation-reduction system due to overload, no proper elimination and nourishment, emotional stress or trauma, discrepancy in circadian rhythm, gut microbiome changes, environmental stress- pollution, chemicals and ultraviolet radiation can increment the production of free radicals. Since there are no enough antioxidants to compensate it, the impermeable structure of cell membrane is broken by lipid peroxidation, no new lipid phosphate turn over happens due to inefficiency in liver. The cell membrane cannot recognize polarity, size or anything, the toxins attached find a space to attack the nucleus and thereby DNA.

DNA methylation is one of the mutagenic changes in most of the autoimmune skin diseases. There are studies to prove that psoriasis, atopic dermatitis, vitiligo has a prior environmental oxidative stress as triggering factor in mutation even though the person is genetically predisposed.

Dooshivisha concept, nearly coincides with this. *Dooshivisha janya rogas* are also triggered by environmental oxidative stress, acharya mentions this as *Pragvata, Ajeerna, Divaswapna* etc. here also, trigger can lead the *Visha* to become active and reach in *Rasathi dhatu* and causing *Kushta* and many other diseases.

The concept '*Kaphavrtham varshagananubhanthi*' (covered by *Kapha*, it remains in the body), may be seen parallel with toxins being depositing on the proteins of the cell membrane, causing protein receptor modification, and breaking its permeability gradually. Toxins enter the cell wall to nucleus and DNA, and cause genetic mutation. Ultimately, the cell loses its structure and function. The function that cell has been doing will be abrupted and this gives rise to many diseases especially autoimmune diseases, because when the cell loses its self-intolerance, it can't distinguish between self and outside.

Therefore, *Susruta's Poorvarupa of Dushivisha* is very much of significance in current scenario, because we can protect the body from autoimmune diseases, by treating *Dushivisha* at early stage itself. By doing *Sodhana*, proper elimination of *Doshas* occurs, and it will regain its dynamic equilibrium, or else, cell membrane can reacquire its dynamic equilibrium in polarity by lipid phosphate turnover. Antitoxic drugs in *Dushivishari agada* are abundant in antioxidant action also, so it can help stabilizing the oxidative stress in the body.

But it should be noted that, these toxins are entering our body daily, there is no way, we can permanently stop it. So, timely *Sodhana* and intake of antioxidants internally and externally can only protect us to an extent from this condition. Any compromise with the diet and regimen can bring back the diseases.

CONCLUSION

It is of very fascination that the umbrella term "*Dushivisha*" can be incorporated in a wide variety of diseases of present era from autoimmune diseases to cancer. Modern Science finds very much difficulty in treating autoimmune disorders, as steroids come to their ultimate help at the end. Steroids come with a lot of side effects in short and long run. So, Ayurveda can come up with an alternative of perceiving autoimmune diseases from the eyes of *Dushivisha* and treating according to it.

No other science has explained the prodromal signs of autoimmune diseases as *Susrutha* explained, as *Poorvarupa* of many diseases, including *Dushivisha*. In modern era, every person is exposed to pollution and chemicals, in one way or other, so this can be taken as the preventive measure to protect us from many diseases in future.

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Cite this article as:

Aswani Krishnan K, Seemaja G. Incorporating Dushivishajanya Rogas to Autoimmune Skin Disorders- Breaking the Cell Membrane Impermeability- A Conceptual Study. *International Journal of Ayurveda and Pharma Research*. 2026;14(3):76-81.

<https://doi.org/10.47070/ijapr.v14i3.3932>

Source of support: Nil, Conflict of interest: None Declared

***Address for correspondence**

Dr. Aswani Krishnan K

PG Scholar,

Department of Agadatantra,

Government Ayurveda Medical College,

Thiruvananthapuram, Kerala.

Email: aswanikrishnan002@gmail.com

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