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### REVIEW OF GARA VISHA AYURVEDA TOXICOLOGY

Dr. Dnyaneshwar Sonba Naykodi

Associate Professor Agadtantra Deptt. Ashvin Rural Ayurved College, Manchihill

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Email: <u>drnaykodids@gmail.com</u>

#### **ABSTRACT**

Human body has the natural tendency to defend itself by eliciting immune response for the maintenance of health. Immune response is recognizing and destroying the antigens of microorganism by triggering the innate immune components such as activation of T-cell or production of antibodies. Sometimes in the sensitive individuals antigens present in the environment produces altered immune response called hypersensitivity. It is manifested with signs and symptoms that are at times lethal. Hapten-carrier adduct behaves as an allergen and induces hypersensitive reactions. Hapten is a small molecule which combines with a large protein, forming hapten-carrier adduct and evokes immune response. Signs and symptoms often with detrimental effect are also found when the body is afflicted with Garavisha

Keywords: Ayurveda, Gara Visha, Antibodies.

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### INTRODUCTION

Karl Landsteiner is the pioneer of the concept of hapten. Haptens are small molecules (<1000 D) that combine with large protein to form hapten-carrier Hapten alone cannot elicit adduct. immune response; even the carrier protein by itself may not produce the same. The hapten-protein combination is the haptencarrier adduct that acts as antigen and binds with specific antibodies or activated to produce immune reaction. Hapten-carrier adduct some time acts as allergen and their exposure primarily occurs through skin surface, oral route, and respiratory tract. The dietary hapten exposure through processed food and formula milk is common nowadays.[3] Notable example of hapten is urushiol which is absorbed through the skin and undergoes oxidation to produce reactive molecule quinone (the actual hapten). Quinone reacts with skin protein to form hapten-carrier adduct which acts as toxin. The first exposure of the body to adduct the hapten-carrier causes sensitization and proliferation of the effect or T-cell, while in the subsequent exposure, the activated T-cell generates immune reaction by producing skin blisters.[4]

# Concept of hypersensitivity

Under normal circumstances, host defense in proper progressive order culminates in well-controlled immune and inflammatory response that protects him/her from offending antigens. The immune response in some person appears as side effect called hypersensitivity.[5] Hypersensitivity is a symptomatic interaction between host

defense and allergen causing exaggerated and harmful response in the body. Hypersensitivity is frequently known as alleray and reaction ranges from mild to life-threatening. It is mainly of two types, immediate hypersensitivity and delayed hypersensitivity.[6] In immediate reactions, hypersensitivity there immediate manifestation of symptoms and is mediated by IgE antibody. The antigen binds to IgE antibodies already attached to the mast cell because of previous exposure to the same antigen. The antigen-antibody reaction releases plenty of histamine and other chemicals from mast cell causing vasodilatation and shock along with other symptoms. Delayed hypersensitivity reaction is mediated by T<sub>H</sub> 1 helper T-cells (T<sub>4</sub> cell). The reaction results in delayed symptoms. In the first exposure, allergen processed by the macrophage is presented to T<sub>4</sub> cell for its activation. In the second exposure, more T₄ cells activated are formed. T<sub>4</sub> cell secretes many chemicals causing activation of more macrophages that destroy the allergen and at the same time, are indurations, redness destruction of healthy tissues in that area. Antigen in the form of allergen introduced for the first time in life in host body is the sensitizing dose and reaction does not occur, but on second exposure, reactions appear.

In the traditional Gell and Coombs system of classification, hypersensitivity reactions are of four types:[7]

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- Type I hypersensitivity reaction is IgE antibody reaction. Atopic allergy with genetic predisposition belongs to this category
- Type II hypersensitivity reaction is cyto-toxic reaction
- Type III hypersensitivity reaction is immunocomplex reaction
- Type IV hypersensitivity reaction is delayed reaction mediated by helper T-cell.

The former classification of two types of hypersensitivity reaction (immediate and delayed) is relevant for the present article.

## The concept of Visha

The word Visha is derived from the root "Vis" by having "Ka" preposition. This means to encompass, pervade, or occupy. The term Visha gets its name from Vishada. Substance that enters and vitiates the healthy Dhatu (structural components, tissues) of the body and may or may not manifest with lethal signs and symptoms is termed as Visha.[8]

Ayurveda describes three varieties of Visha, i.e., Jangama (animal origin), Sthavara (plant and mineral origin) and Kritrima (artificial poison).[9]

The third variety of poison is prepared by the combination of different materials. When it is produced by the combination of two nonpoisonous materials, it is called *Garavisha*; while combination of two poisonous materials forms *Kritrima Visha*.[10]

### The concept of Garavisha

The word Gara is derived from root word "Gri" with the suffix "Ac." This means diluted or reduced in potencies.[11]Garavisha is a combination of two nonpoisonous substances. It slowly produces toxic effect by vitiatina the Dhatu (structural components of the body). This is followed by manifestation of mild to drastic clinical features. Unlike other poison, it does not cause instantaneous death. Garavisha commonly enters body through food preparations.[12] By nonpoisonous, it means that ingredient forming Garavisha when enters the body separately does not produce any symptom, but their combination effect producing poisonous clinical features such as laziness, heaviness of the body, cough, dyspnea and edema that appear after 15 days or 1 month duration of affliction.[13] There are ten attributes of Visha.[14] These are equally applicable for Garavisha but are of Alpa Virya (mild intensities).

Garavisha is а combination of nonpoisonous components (substances) producing signs and symptoms of Visha after application or consumption. Hapten-carrier adduct is combination of two components, hapten and carrier protein. As a single component hapten or carrier protein does not function as immunogen and cannot elicit immune response.

Single component of Garavisha also does not produce Visha (toxic) effect. They produce toxic effects on combination. The combining substances



forming Garavisha may be of Viruddha Veerya (mutually contradictory potencies) obtained from Viruddha Ahara and other sources of Viruddha. The resultant reaction of two mutually contradictory potencies is adverse for the body hence, Garavisha is a toxin and behaves as an allergen. The hapten and the carrier protein do not produce immunogenic effect separately, but their combination as hapten-carrier adduct makes them bind to the antigen presenting cell for activation of T- and B-cells and produce harmful immune reaction. Hence, Garavisha has a striking similarity with the hapten-carrier adduct.

Garavisha like varieties other of Visha causes Vishada or stressful condition. It is of slow reacting nature and gradually produces toxic effect by vitiating Dhatu through formation of Amadosha and Agnimandya, while exposure to hapten-carrier adduct causes sensitization and proliferation of effector T-cells and antibodi es present in the body, and on subsequent exposure, sometimes, stressful immune response is triggered at the site (tissues) of sensitization activated memory T-cell antibodies. The stressful immune response is the adverse effect of body's defensive mechanism and is called hypersensitivity. of Garavisha is The reaction comparable to hypersensitive response to body's immune mechanism.

In immediate hypersensitivity reaction, response is seen within 12 h of antigen challenge to preformed antibodies. Atopic allergy with genetic predisposition (allergy running in the family) produces immediate

hypersensitive response with symptoms manifesting within few minutes to few hours. Symptoms appear after 2-4 weeks due to Garavisha affliction. In Ayurvedic treaties, Garavisha poisoning is included under Kulaja Vyadhi. Immediate hypersensitivity reaction along with atopic does not match with the allergy characteristic result of Garavisha and so cannot be included under its ambit.

Kalantara Vipaka[28] implies delayed reaction of Garavisha. It takes time for such poison to get metabolized and produce toxic effect. This feature to delayed hypersensitivity common reaction that takes few days to week for the development of symptoms. Garavisha is analoaues to hapten-carrier adduct that can produce delayed hypersensitivity.

The concept of hapten-carrier adducts and delayed reaction hypersensitivity existed in the Ayurvedic treaties centuries ago and the terms Garavisha was applied for it. Clinically, hapten-carrier adduct and Garavisha produce more or less same type of clinical manifestation and systemic involvement. This aroused the necessity to relate Garavisha with hapten-carrier adduct. Further comprehensive analytical studies are necessary establish the concept of Garavisha with hapten and hapten-carrier adduct which may open new dimensions to understand the concept of Garavisha.

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