International Journal of Education and Science Research Review
E-ISSN 2348-6457
Volume-10, Issue-4 July-August-2023 P-ISSN 2349-1817
www.ijesrr.org Email- editor@ijesrr.org

ANTIHISTAMINE ACTIVITY OF SOLANUM XANTHOCARPUM

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ABSTRACT

A number of physiological processes, such as immunological responses and inflammation, rely on histamine-mediated allergic reactions. The anti-inflammatory effects of the medicinal herb Solanum xanthocarpum have long made it popular in many parts of the world. Through experimental tests, this study sought to evaluate Solanum xanthocarpum's possible antihistamine activity. We conducted a battery of pharmacological tests to determine the antihistamine effects of Solanum xanthocarpum aqueous and ethanolic extracts. The phytochemical content of the extracts was also studied in order to find any bioactive chemicals that might be responsible for the effects that were observed. The results of this study provide credence to the long-standing belief that Solanum xanthocarpum has antihistamine properties, which would explain its historic usage in the treatment of inflammatory disorders. It is necessary to isolate and characterise the discovered bioactive chemicals further since they may be responsible for the observed effects.

Keywords: *histamine play, Solanum xanthocarpum, immune responeses.*

INTRODUCTION

"Solanum xanthocarpum" is a species of plant that belongs to the Solanum genus and is referred to by its own botanical name. The specific botanical specimen that is referred to as Schrad and Wendl is a perennial herbaceous plant that is defined by its prickly nature and dispersed growth pattern. It is a member of the family Solanaceae. Yellow Berried Nightshade is a popular name for this brilliant green plant, which is also known by its indigenous name, Kaṭṭakari. It is generally known for its vibrant green appearance. The specific species in question has a base that is composed of wood and may grow to heights of two to three meters. The majority of its growth occurs in dry areas, such as roadsides and uncultivated plains, where it often takes the form of a weed. It is extensively dispersed over the whole of India.

Dasamula is a collection of ten medicinal plants that are commonly used in the practice of Ayurveda. This specific ingredient happens to be a member of the dasamula category. There are a great number of significant qualities that are shown by the botanical specimen in question. It is characterized by a quality that is caustic and features a flavor that is quite bitter. Furthermore, it has thermogenic qualities, which means that it is able to create heat inside the body for the purpose of consumption. Additionally, this plant has anthelmintic properties, which add to its effectiveness in removing parasitic worms from the organism that it is being used to treat. In addition to this, the plant has anti-inflammatory effects, which demonstrates the It has been discovered that the botanical specimen in issue has a variety of chemical ingredients, including, among other substances of a similar kind.

Both India and China have a long and illustrious history of using botanical resources into their respective healthcare systems. This history is both rich and vast. One of the most ancient forms of knowledge is the practice of Ayurveda, which originated about the year 1500 B.C. and is considered to be one of the oldest medical practices. The essay sheds light on the fact that the renowned pharmacopoeia of India contains data that have been thoroughly maintained and belong to herbal medications. This compendium contains a comprehensive collection of monographs that provide information on the safety standards of medicinal plants and the standardized formulations of herbal medications.

The country of India is home to a rich biodiversity, which includes an outstanding collection of over 7500 medicinal plants. These species include both herbs and weeds. Among this enormous collection, there is a notable subgroup of two thousand plants that have been recognized for their priceless therapeutic capabilities. These plants have been especially useful in the treatment of infectious illnesses, metabolic problems, and immunological diseases that impact both people and animals. Both the Chraka Samhita and the Sushruta Samhita are considered to be two of the most important works in the field of traditional Indian practice of medicine.

Over the course of the last several decades, there has been a significant increase in the usage of traditional medical systems in both industrialized and developing countries. At the present day, these systems make up a significant fraction of the healthcare systems that are found all over the world. It is important to remember that around 70–80 percent of the population of undeveloped and emerging countries, such as those located in Africa and Asia, including India, is dependent or dependent on the government. There has been a discernible increase in the employment of complementary and alternative medical systems in recent years. The inclusion of medicinal plants into diets as dietary supplements and as a way of treating degenerative and incurable diseases has been adopted by around sixty to sixty-five percent of the population in these nations.

From this point forward, it is of the utmost importance to underline the requirement of a surge in academic inquiry in order to strengthen the basis of data about the efficacy and safety of treatments that are founded in traditional medicine. In addition, it is of the utmost importance to encourage the development of appropriate research procedures and techniques in order to assess the efficacy of the aforementioned medicines in the treatment of a variety of infectious illnesses, metabolic disorders, immunological disorders, and autoimmune diseases.

According to the findings of a research that was carried out by Nguyen and colleagues in the year 2010, it has been noted that a sizeable percentage, namely forty percent, of the population in the United States is affected by certain respiratory ailments. It is notable to see a considerable rise in the occurrence of immunomodulated respiratory infections in India. This is something that should be taken into consideration. To be more specific, it has been proven by Murthy and Sastry in 2005 and by Paramesh in 2002 that around 18% of the population in India suffers from asthma. This information was gathered from the research conducted by both of these researchers. Due to the unfortunate conditions that now exist, our group has decided to conduct an inquiry into the possibility of using herbal medicine as a feasible option for reducing respiratory problems that are caused by immunological disorders that are induced by allergens among the Indian population. When it comes to the development of asthma and other immunological respiratory issues, it is commonly believed that persons who have a deficit in innate anti-inflammatory activity are more likely to be vulnerable to the development of these conditions. For the purpose of addressing the widespread

occurrence of respiratory disorders that are caused by proinflammatory molecules, it is of the utmost importance to conduct a thorough investigation of medicinal herbs that have been widely recorded in Ayurveda and other ancient systems. Utilizing these herbs for the aim of treating respiratory diseases that have developed as a result of infectious agents and weakened immune functioning has been a common practice throughout history explained by Suresh et.al.(2019),Singh et.al.(2010), Abbas et.al.(2014) and Onlia et.al (2018).

It has been found, after conducting a comprehensive examination of the relevant literature, that Solanum xanthocarpum, which belongs to the Solanaceae family and the Solanum genus, has been selected as the topic of inquiry in order to investigate the therapeutic qualities of the plant on a molecular level. In accordance with the recommendations that have been developed, which stress the significance of evaluating both the effectiveness and the safety of the treatment, this choice has been brought about. Regarding the therapeutic usefulness of this drug in connection to its role in immunomodulation within signal network pathways, there is a paucity of information that is currently available. Taking into consideration the present status of scientific research, it is clear that there is a significant dearth of clinical-based investigations. Surprisingly, no conscientious researchers have taken on the challenging task of investigating the complex mechanisms by which biomolecules regulate signal pathways. This is particularly relevant in relation to the monitoring of the delicate immunological equilibrium throughout the development and progression of respiratory ailments and a variety of other disorders.

OBJECTIVE

1. To Look into the solanum xanthocarpum's antihistamine properties.

2. To use instrumental analysis of the experimental medicine to determine the elemental content, functional group composition, and particle size.

RESEARCH METHODOLOGY

Gathering Of Vegetation

The Solanum xanthocarpum (SX) plants, which were gathered during the months of February and March in the vicinity of Mathura, India, underwent identification and authentication procedures under the expertise of Dr. Anuradha Upadhye from the esteemed Agharkar Research Institute in Pune. This authentication process was assigned the deposition number 26 in the records maintained by Dr. Upadhye. The entire botanical specimen, encompassing both the blossoms and the rest of the plant, denoted as SX, underwent a process of desiccation through exposure to a shaded environment. Subsequently, the dried material was subjected to mechanical comminution, resulting in a coarse powder. A quantity of 200 grammes of SX in powdered form was employed for the purpose of conducting a hot aqueous extraction utilizing the soxlet apparatus. The extraction process was carried out at a temperature of 1000C for a duration of 8-10 hours. The solution that was obtained was subjected to the process of drying through the utilisation of a rotator evaporator. Subsequently, the percentage yields of the resulting product were determined through meticulous calculations. The extraction of the entire plant was conducted over a series of successive years, during which the average yield of HAESX was quantified.

$$\% \text{ yield} = \frac{\text{Wt. of extract}}{\text{Wt. of powered materials}} \times 100$$

Isolates of bacteria

The fungus Candida albicans, which are housed within the microbiology laboratory of the Biotechnology department, were employed for the purpose of investigating the antimicrobial properties of the HAE (hexane extract) derived from Solanum xanthocarpum (referred to as HAESX). Before delving into the examination of these bacterial cultures and the culture of C. Albicans, it was imperative to conduct a comprehensive characterization based on various factors such as morphology, cultural attributes, and biochemical characteristics. This characterization process was meticulously outlined by Cruickshank in 1975. The utilisation of a Salmonella typhimurium culture was additionally employed in the production of somatic (O) antigen, which was subsequently utilised for the examination of the humoral immune response.

Animals used in experiments

During the course of the experiment, both male and female Wistar albino rats which ranged in weight from sixty to one hundred grammes were used. The GLA University, which is the most prominent animal home in Mathura, is where these rats were born and nurtured. A registration number of GLAIPR/CPCSEA/IAEC/2014/Biotech02 has been assigned to this establishment. In addition to a wide range of haematological and biochemical blood parameters, the researchers wanted to get a deeper understanding of humoral and cell-mediated immune responses. In addition, we examined the rise in the number of splenocytes and the production of cytokines such interleukin-2, interleukin-4, interleukin-10, interferon-gamma, and tumour necrosis factor-alpha.

The Wistar rats utilised for the study were acquired from the animal house facility of the Institute. The subjects were accommodated within polypropylene enclosures, with a total of six organisms per enclosure. These enclosures were situated in a climate-controlled environment, maintaining a temperature of 25 ± 2°C. Additionally, the subjects were exposed to a light and dark cycle of 10:14 hours, while the relative humidity was maintained at a range of 45-55%. The subjects were provided with Nutrimix Std. 1020, a laboratory animal diet manufactured by Nutrivet Life Sciences located in Pune, India. Additionally, they had unrestricted access to Aquaguard-purified water for their hydration needs. The sustenance, albeit excluding the aqueous component, was duly withheld for a duration of three hours preceding the commencement of the experiment.

Residing

The experimental animals were accommodated within enclosures containing bedding composed of paddy husk and grass. The experimental animals were provided with standard laboratory rodent food (Hindustan Animal Feeds) and the provision of unrestricted access to potable water. The subjects were diligently upheld in accordance with the established guidelines stipulated by the esteemed Animals. as described by Burman and Mendl (2004). Only animals that exhibited good health were selected for participation in various experiments. The marking of each individual animal was accomplished through the utilisation of a solution consisting of 1% picric acid and crystal violet.

Tools for phytochemical analysis

The reagents that we shall discuss are Mayer's reagent, Hager's reagent, Dandruff's reagent, the Ninhydrin test reagent, Ferric Chloride solution, the Alkaline test reagent, the Biuret test reagent, and Legal's test reagent. The experimental procedure involved the utilisation of various reagents, namely pyridine, alkaline sodium nitroprusside, and methanol from reputable suppliers such as Himedia/SRL.

Materials for the Expression of m-RNA

The experimental materials utilised in this study encompassed TRI reagent (manufactured by Sigma), Chloroform, Isopropanol, 75% Ethanol, Nuclease free water (obtained from Himedia), Reverse transcriptase, and a Real time PCR Kit (provided by Thermo scientific). The experimental setup includes the utilisation of several key components. These components consist of IL10, IL-2, Oligo (dT)18 primer at a concentration of 100 pmole, Primer obtained from Xcelris USA, and Avian Myaloblast Virus (AMV) reverse transcriptase sourced from Thermo scientific.

Individual bacteria

The Bacillus subtilis microbes (MTCC-441), Phytoplankton us aureus (MTCC-9760), Escherichia coli (MTCC-1563), Pseudomonas aeruginosa (MTCC-8076), and the fungus Candida albicans, which are housed within the microbiology laboratory of the Biotechnology department, were employed for the purpose of investigating the antimicrobial properties of the HAE (hexane extract) derived from Solanum xanthocarpum (referred to as HAESX). Before delving into the examination of these bacterial cultures and the culture of C. Albicans, it was imperative to first characterize them based on their morphology, cultural attributes, and biochemical characteristics, as expounded upon by Cruickshank in 1975. The utilization of Salmonella typhimurium culture was additionally employed in the preparation of somatic (O) antigen for the purpose of investigating the humoral immune response.

Plant Stuff

Careful attention was paid to the development of the plant material, which was derived from indigenous plants in the Satara region of Maharashtra. The botanical material has been legally recognized by the famous Botanical Survey of India, which is a respected organization located in Pune and it comes under the authority of the Ministry of Environment and Forests of the Indian government.

Materials and chemicals

The experimental materials utilised in this study encompassed surgical sutures procured from Johnson and Honson Ltd., an esteemed establishment based in India. Distilled water, an essential component, was employed in conjunction with carrageenan sourced from Thermoses, Fine Chem., India. Histamine, a crucial substance, was obtained from Research Lab Fine Chemical, India. Ethanol, a commonly utilised solvent, was also included in the experimental setup. The paleothermometer employed in this investigation was the Orchid Scientific PLM02, a reputable instrument originating from India. Surgical cotton, an indispensable material, was acquired from Mamta Surgical Cotton Industries, India. Lastly, an aesthetic ether, a vital compound, was obtained from Rachana Ether Pvt. Ltd, India.

Abridged

The plant material of S. xanthocarpum was gathered and subsequently fragmented into small segments. These fragments were then subjected to a process of desiccation under a shaded environment, resulting in the production of a coarse powder. This powder was generated through the utilization of a pulverizing apparatus. The granular substances underwent an extraction process utilizing ethanol via the Soxhlet apparatus. The collected extracts were subjected to evaporation under atmospheric pressure, ensuring the removal of any remaining solvents through in-vacuo techniques. The extract that had been prepared was employed for the purpose of conducting a screening process to evaluate its potential anti-inflammatory activity.

Acceptance of the study plan

The determination of an appropriate dosage and the formulation of a dosage form for the purpose of pharmacological screening is a critical aspect of experimental design.

The initial dosages were chosen in accordance with the findings of the comprehensive literature review and the outcomes of the acute toxicity investigation. In the absence of any such reference within the literature, it was determined that the maximum dose for the preliminary study would be 10 times less than the lethal dose 50% (LD50). Furthermore, two additional doses, each ½-log lower than the maximum dose level, were chosen for the subsequent investigation. The appropriate dosage forms of the extract were prepared on the day of the experiment.

Methods

Analysis and research of acute toxicity trials is the focus here. This research looked at the effects of acute oral toxicity. (AOT) carried accomplished the extraction in conformity with the standards established by the Organization for Economic Co-operation and Development. (OECD), specifically adhering to the principles set forth in guideline 425. The administration of the extract was carried out at a dose limit of 2000 mg/kg. The animals were subjected to individual observation on multiple occasions within the initial 30-minute period following administration. Subsequently, periodic observations were conducted throughout the initial 24-hour timeframe, with particular emphasis placed on the first 4 hours. Following this intensive monitoring period, daily observations were carried out for a total duration of 14 days, with the aim of detecting any signs of toxicity or mortality, if present. The LD50 was determined through the utilisation of the OECD 425 (AOT) software.

The experimental procedure involved the induction of paw edoema in rats through the administration of carrageenan. The male Wistar rats, weighing between 225-250 g, were subjected to a 12-hour fasting period during which they were denied access to food. However, they were provided with unrestricted access to water prior to the administration of drugs. In order to provide a more precise explanation, ten minutes had passed as a result of the oral administration of diclofenac sodium (10 mg/kg p.o.) or a test medication (10, 30, and 100 mg/kg p.o.). Afterwards, a newly made suspension of 0.1 milliliters of 1% carrageenan was injected into the subplantar tissue of the right hind paw of each rat. This was done without any prior preparation. It was done following the step that came before this one. The Plethysmometer (Orchid Scientific PLM02) was used to collect plethysmographic measures of inflammation at intervals of half an hour, one hour, two hours, four hours, eight hours, and twenty-four hours after the administration of carrageenan.

These measurements were taken throughout the course of the experiment. There was a modification made today to the computation of the volume of the paw.

The experimental procedure involved the induction of paw edoema in rats through the administration of histamine. A sub-plantar injection of histamine, specifically 0.1 ml of a 1% solution, was administered to the rat paw. This injection was performed one hour subsequent to the oral administration of either the vehicle, the test drug, or diclofenac sodium, as part of the inflammation induction procedure. The measurement of inflammation was conducted plethysmographically utilising a plethysmometer, specifically the Orchid Scientific PLM02 model. This measurement was performed at three distinct time intervals: immediately following histamine injection, as well as at half an hour and one hour post-injection.

The experimental study conducted involved the induction of granuloma in rats through the utilisation of cotton pellets. A cohort of male Wistar rats, weighing between 225 and 250 grammes, was carefully chosen for this study. These rats were subsequently allocated into five distinct groups. In preparation for the experiment, a period of 12 hours was designated during which sustenance was deliberately restricted, while water was made readily available for consumption. The animals were administered with a vehicle, a test drug at a dosage of 100 mg/kg orally, or diclofenac sodium. The administration of anaesthesia was initiated in the animal by means of anaesthetic ether, precisely one hour subsequent to the initial dosage administration. In this experimental procedure, a sterile cotton pellet with a mass of 20 mg was carefully placed within the subcutaneous tissue of each scapula region in rats. This was achieved by making small incisions to ensure precise insertion. The administration of the drug was sustained for a duration of seven consecutive days. On the eighth day of the experiment, the animals were subjected to an excessive administration of anaesthesia, resulting in their demise. The cotton pellets were carefully extracted, meticulously measured, and subsequently placed within a controlled environment of a hot air oven set at a temperature of 60°C. This process was continued until a state of equilibrium was reached, indicated by the attainment of a consistent weight.

RESULT AND DISCUSSION

The induction of edoema in the rat paw of the control group was achieved through the subcutaneous injection of a 0.1 ml solution containing carrageenan at a concentration of 1% in the sub-plantar region. The administration of S. xanthocarpum extract (SxE) at doses of 10, 30, and 100 mg/kg orally, one hour prior to carrageenan induction, did not exhibit any discernible anti-inflammatory activity across all observed time intervals.

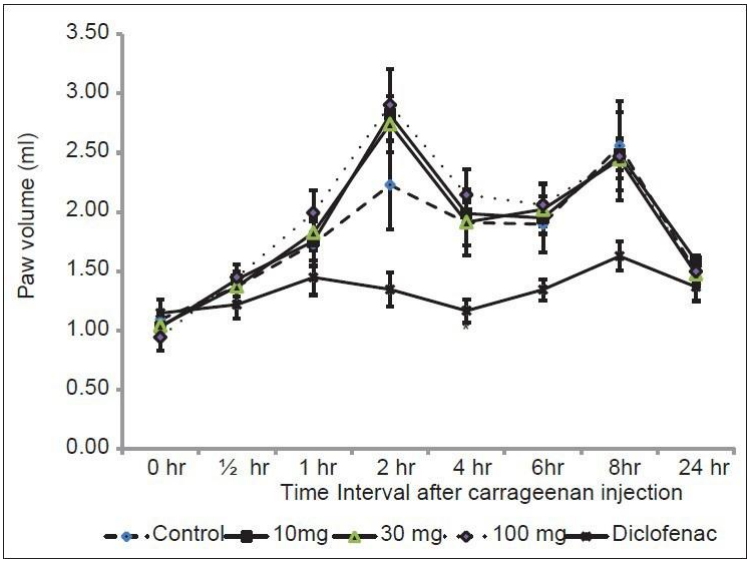

Figure 1 Rats' paw edoema caused by carrageenan and the impact of Solanum xanthocarpum ethanol extract

The administration of diclofenac sodium resulted in a reduction of inflammation across all time intervals. However, it is noteworthy to mention that a statistically significant decrease ($P < 0.05$) was solely observed at the 4-hour mark, as depicted in Figure 1.

Rats with histamine-induced paw edoema

The administration of histamine subcutaneously in the rat paw elicited a notable inflammatory response in the control group. The administration of SxE at doses of 10, 30, or 100 mg/kg orally did not yield any noteworthy alterations in paw volume, as depicted in Figure 2.

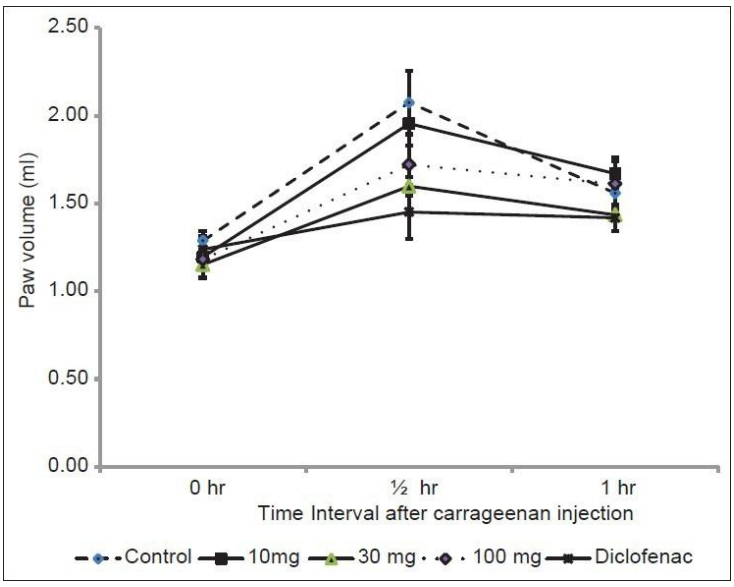

Figure 2 Rat paw edoema caused by histamine: the impact of Solanum xanthocarpum ethanol extract

Granulomas in rats causing cotton pellets

The administration of the drug SxE at a dosage of 100 mg/kg orally exhibited a notable ability to mitigate the inflammatory process associated with the formation of granulomas in rats. This effect was observed after a treatment duration of 7 days, as evidenced by a reduction in both the wet and dry weights of the cotton pellets. This data is presented in Table 1, highlighting the significant impact of SxE on suppressing granuloma formation. Nevertheless, it is important to note that the decrease in weight of the pallet in both instances did not exhibit a significant magnitude. The administration of diclofenac sodium at a dosage of 10 mg per kilogramme orally exhibited a significant reduction in the size of the granuloma, as indicated by a statistically significant p-value of less than 0.05.

Table 1 Rat cotton pellet granuloma as a result of S.xanthocarpum ethanol extract

Treatment (mg/kg, p.o.)	Wet weight (mg)	Percentage inhibition	Dry weight (mg)	Percentage inhibition
Control	293±22.04	-	148±8.16	-
Extract (100)	277±19.59	5.46	135±13.8	8.78
Diclofenac (10)	229*±12.65	21.84	85**±10.61	42.56

S.xanthocarpum: *Solanum xanthocarpum*, *$P<0.05$; **$P<0.01$

DISCUSSION

Edoema in the rat hind paw caused by carrageenan is the principal test for anti-inflammatory drugs that is utilised the most often. The biphasic occurrence of carrageenan-induced edoema in the rat paw was reported by Vinegar et al. (1969) as consisting of an early phase and a late phase. In the first stage, histamine, serotonin, and bradykinin are released, while in the second stage, prostaglandins are formed. Furthermore, in the latter stages of inflammation caused by carrageenan, neutrophil infiltration and the generation of free radicals such as hydrogen peroxide, superoxide, and hydroxyl radicals by neutrophils are involved. Edoema caused by carrageenan also involves the enzymes cyclooxygenase and lipoxygenase. Inhibiting the release of early mediators, such histamine and serotonin, may explain the suppression of the first phase, whereas inhibition of cyclooxygenase may explain the activity of the second phase.

In this investigation, we found that SxE at 10, 30, and 100 mg/kg did not alleviate carrageenan-induced inflammation. At 4 hours, diclofenac sodium significantly reduced inflammation, lending credence to its well-established method of inhibiting the cyclooxygenase pathway. An essential mediator of inflammation, histamine has strong effects on vasodilation and vascular permeability. Inflammation may be mediated by a variety of inflammatory substances, one of which is histamine H1 receptors. A well-established paradigm for studying inflammation and neutrophil infiltration in paw tissue is histamine-induced paw edoema. The control of neutrophil recruitment is regulated by histamine, according to many findings. This is true both on its own and in combination with chemo-attractants including platelet activating factor, interleukin 8, and leukotriene B4.

CONCLUSION

Experts and botanists from Gunapadam were able to identify and verify the experimental medicine. Using traditional procedures, the experimental medication was produced and subjected to purifying steps. Toxins may be removed during the drug purification process, making the medicine more effective. Grinding also changes the drug's particle size, which increases its bioavailability. Glycosides, saponins, carbs, phytosterol, phenols, triterpenes, and protein are among the chemicals identified by phytochemical examination of the medicine. In the treatment of chronic inflammatory illnesses such bronchial asthma, plant steroids are essential. Studies have shown that glycosides may ameliorate allergic inflammation and decrease eosinophil formation in tissues. Damage to the epithelial tissue in asthma was remedied by carbohydrates. The secretion of mucus from the lungs is accelerated by saponins.

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