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ORIGINAL ARTICLE

Anti-Inflammatory and Antiallergic Activity of Arbutin against Ovalbumin-Induced Allergic Rhinitis in Mice through the Modulation of Inflammatory Responses

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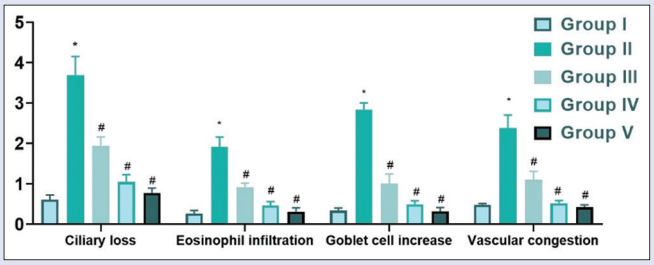
ABSTRACT

Background: Allergic rhinitis (AR) is the prevalent inflammatory disease in the airway due to allergic reactions in response to numerous allergens. AR is considered as a type-I allergic condition and proceeded as early- and late-phase hypersensitivity. **Objectives:** In the existing work, we scheduled to discover the anti-inflammatory potential of arbutin against the ovalbumin (OVA)-provoked AR in mice through modulation of inflammation. **Materials and Methods:** The AR was triggered to the BALB/c mice by injecting 500 µL of OVA sensitization solution and then treated with the arbutin (25 and 50 mg/kg, respectively). Dexamethasone was used as standard. The occurrences of sneezing and nasal rubbing were detected within 15 min after the last OVA challenge. The status of OVA-specific immunoglobulin E (IgE), histamine, and malondialdehyde (MDA) was scrutinized by using assay kits. The status of NF-κB/IκBα and STAT-3 signaling molecules and its related cytokines was considered by using assay kits. The histological scores were evaluated by the histological alterations. **Results:** The arbutin supplementation lessened the incidence of nasal rubbings and sneezing, OVA-specific IgE and histamine, and MDA status. The arbutin-administered AR mice established the appreciable reduction in the NF-κBp65, phosphorylated IκBα, interleukin (IL)-1β, and tumor necrosis factor-α levels, also improved the IκBα status in the AR mice. Arbutin reduced the STAT-3, phosphorylated STAT-3, RORc, IL-17A, IL-5, and IL-6 levels and elevated the IL-10, IL-12, and IFN-γ status. Arbutin supplementation to the AR mice exhibited the considerable amelioration of the histological scores of OVA-provoked AR mice. **Conclusion:** Our results established that the arbutin treatment effectively ameliorated the OVA-provoked AR in mice through the modulation of inflammation, and it could be auspicious therapeutic agent to treat the RA.

Key words: Allergic rhinitis, arbutin, inflammation, NF-κB/IκBα pathway, ovalbumin

SUMMARY

- Allergic rhinitis (AR) is an extensive inflammatory illness in the airway due to allergic reactions in response to the numerous allergens
- Arbutin palpably reduced the nasal symptoms, ovalbumin-specific immunoglobulin E, and histamine in the AR mice.



Abbreviations used: AR: Allergic rhinitis; OVA: Ovalbumin; IgE: Immunoglobulin E; MDA: Malondialdehyde.

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INTRODUCTION

Allergic rhinitis (AR) is the most predominant inflammatory disorder that befalls in the airway due to allergic reactions in response to numerous allergens. The pervasiveness of AR is stated to be 10% of the total global population. AR is provoked in the nasal membrane due to the response to environmental allergens interacting with immunoglobulin E (IgE).[1] AR is not lethal, but disturbing marks such as sneezing, nasal congestion, and itching reduce the patient's life quality.[2] These marks were caused by the inflammatory and allergic regulators discharged from eosinophils, basophils, epithelial cells, lymphocytes, and mast cells that were complicated in adaptive and innate immunity.[3] AR is observed as a risk factor of asthma. AR is considered as a type-I allergic condition and is illustrious by watery rhinorrhea, nasal blockage, and repetitive sneezing. AR is proceeded as an early- and late-phase hypersensitivity.[4] During the early phase, antigens entered via nasal mucosa pass through the epithelial cells and bind to the IgE antibodies of the mast cells. Due to the response to the antigen–antibody reaction, the mast cells release the chemical regulators, e.g., histamines. These mediators annoy the endings of sensory nerves and blood vessels of the nasal mucosa that finally produce mucosal swelling, watery rhinorrhea, and sneezing. During the late phase, diverse inflammatory cells such as lymphocytes and mast cells penetrate into the mucosa and more deteriorate the condition through the chemokines, cytokines, and chemical mediators.[4]

Inflammation is an imperative immune process to injury and/or infection in the body, which aids in upholding tissue homeostasis in strained situations.[5] It was stated that the transcription factors

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such as STAT-3, NF-κB, inflammatory enzymes and cytokines, e.g., COX-2, MMP-9, tumor necrosis factor (TNF)-α, interleukin (IL)-1, IL-6, IL-8, and chemokines are the critical molecular regulators of the inflammatory conditions. Among these regulators, NF-κB, a ubiquitous transcription factor, is a prime regulator of inflammation as it arbitrates the huge arrays of genes encoding cytokines and its receptors and cell adhesion molecules, which were complicated in the progression of inflammation.[6] Furthermore, the IL-4, IL-5, and IgE expressions were drastically increased in the AR patients, while the expression of IL-10 is diminished.[7] The immune cells such as eosinophils, basophils, lymphocytes, and mast cells are caused via activation with the allergens and IgE complex.[8]

NF-κB mediates the expression of inflammatory regulators, and the overexpression of the cytokines such as TNF-α could fallout in the frequent diseases. Enhancement of IL-1, IL-6, IL-8, and TNF-α was exposed to play an imperative function in oxidative stress, which results in inflammation.[9] IgE secreted by Th2 cells binds to the IgE receptors on the mast cell surface to sensitize the cells, which leads to the release of leukotrienes and histamine that incite the AR.[10] The IL-4 and IL-13 accreted via stimulated Th2 cells were known as the bossy regulators of the pathological progression of AR.[11] Moreover, IL-17 and IFN-γ are proinflammatory regulators accreted by Th2 cells, which could exacerbate the mucosal protein and cytokine expressions. IFN-γ and IL-17 play a central role in the progression of AR.[12]

The existing therapeutic tactics for the AR contain administration of intranasal corticosteroids and antihistamines.[13] It was related to the retardation of psychomotor function, sedation, and condensed performances.[14,15] Moreover, the prolonged administration of steroids could produce adverse belongings such as throat irritation, headache, and nasal dryness.[16] Hence, the examination of therapeutic targets with both safety and effectiveness for AR management is indispensable.

Arbutin is a glycosylated hydroquinone, which is isolated from bear-berry plant in the family of *Ericaceae*. Earlier studies exposed that arbutin influenced the many biological benefits such as anticancer activity,[17] antimicrobial activity,[18] and anticonvulsant activity.[19] It was stated that arbutin is a potent antioxidative, cytoprotective, and anti-inflammatory agent.[20-22] However, the therapeutic role of AR was not systematically studied yet. Hence, in this existing work, we tried to discover the anti-inflammatory potential of arbutin against the ovalbumin (OVA)-provoked AR in mice through the modulation of inflammation.

MATERIALS AND METHODS

Chemicals

Arbutin, OVA, and other chemicals were accomplished from Sigma Aldrich, USA. The assay kits for the histamine and IgE were acquired from Elabscience, UK. Malondialdehyde (MDA) assay kit was attained from MyBioSource, USA. All the assay kits for signaling molecules and inflammatory cytokines were achieved from R&D Systems, Minneapolis, USA.

Experimental animals

Roughly 6–7 weeks aged BALB/c mice were obtained from the institutional animal house, and the same was continued beneath the specific hygienic laboratory situations at 24°C–26°C temperature with 50%–60% air dampness and 12-h diurnal cycles. All animals were kept adapted for 1 week before the initiation of experiments.

Allergic rhinitis model establishment and treatment

The mice were explained by the sensitization solution, which contains 1 g of aluminum hydroxide and 50 mg of OVA to provoke the allergic response. Sensitization was performed via administering the 500 μL of sensitization solution through intraperitoneal injection on days 1, 3, 5, 7, 9, 11, and 13. Followed by sensitization, the animals were isolated into five groups. Control group received the standard diet without any treatments. Group II animals were OVA-provoked AR group. Groups III and IV were AR animals supplemented with 25 and 50 mg/kg of arbutin, respectively, and Group V animals were administered with 2.5 mg of standard drug dexamethasone (DEX). All the treatments were sustained for 1 week, i.e., from 14th to 21st day.

Assessment of allergic signs

Nasal signs were inspected via counting the incidences of repetitive sneezing and nasal rubbings. The frequencies of sneezing and nasal rubbing within 15 min after the last OVA administration were pragmatic by two observers blinded to the experimental situations.

Determination of ovalbumin-specific immunoglobulin E and histamine

Followed by the animal scarification, the blood was drawn in the clean bags, and the serum was collected. The status of OVA-specific IgE and histamine was scrutinized with the help of ELISA assay kits as per the manufacturer's protocols (Abcam, UK).

Determination of malondialdehyde

The MDA status in the serum of both control and experimental animals was explored with the help of commercial assay kits as per the manufacturer's protocols (MyBioSource, USA).

Quantification of cytokines levels

The nasal lavage fluid was congregated from the animals, and the supernatant was separated via centrifuging and used for the measurement of cytokines. The status of inflammatory mediators, i.e., TNF-α, IL-1β, IL-17A, IL-5, IL-6, IL-10, IL-12, IFN-γ, and RORc, and signaling molecules, i.e., STAT-3, NF-κB, phosphorylated NF-κBp65 (p-NF-κBp65), IκBα, and phosphorylated IκBα (p-IκBα), was scrutinized with the aid of commercial assay kits (R&D Systems, USA). All the examinations were implemented in a triplicate manner. The control and sample suspensions were loaded onto the 96-well plate that was prior coated with a target cytokine antibody and then incubated for 2 h at 37°C. Followed by incubation, each well was aspirated and cleansed four times, and then, horseradish peroxidase was loaded to every well. Finally, the absorbance was taken at 460 nm for the finding of target molecules status.

Determination of histological scores

The nasal mucosal tissues were collected from experimental animals and treated with saline. Then, the tissues were sliced at 5 μm size, then reassigned to glued slides, and dehydrated at 37°C for 12 h and then at 60°C for 30 min. The dehydration and deparaffination of the slides were completed through xylene immersion. Then, the slides were stained with hematoxylin and eosin. Finally, the samples were scrutinized with the aid of the microscope, and the severity of variations scored by a viewer was arranged. The microscopic tissue segments were explored to detect the ciliary loss, vascular congestion, and penetration of inflammatory cells, and the histopathological scores were planned and characterized as graphical images.

Statistical analysis

Data were studied by using the GraphPad prism software (GraphPad, San Diego, CA). Data were depicted as mean ± standard deviation of triplicate values. One-way ANOVA afterward DMRT analysis was done to assess the disparities between groups. The significance level was fixed at $P < 0.05$.

RESULTS

Effects of arbutin on the nasal symptoms of allergic rhinitis mice

The incidences of nasal indications, i.e., repetitive sneezing and nasal rubbing, were raised in the OVA-provoked AR mice (Group II), whereas the control animals (Group I) did not present any nasal symptoms [Figure 1]. In contrast to Group II, the arbutin (25 and 50 mg/kg)-supplemented animals showed the weakened frequencies of nasal rubbings and sneezing (Groups III and IV). The 50 mg/kg of arbutin effectually prevented the nasal symptoms and set near to normal. The standard drug DEX-administered animals also reduced the sneezing and nasal rubbing in the AR mice [Figure 1].

Effect of arbutin on the ovalbumin-specific immunoglobulin E and histamine status in the serum of allergic rhinitis mice

The status of OVA-specific IgE and histamine was extremely raised in the serum of untreated OVA-challenged AR mice, which is a distinction to the control [Figure 2]. Fascinatingly, the arbutin (25 and 50 mg/kg)-supplemented AR mice showed a noticeable diminution in the status of OVA-specific IgE and histamine in the serum. The DEX administration also revealed the appreciable lessening in the IgE and histamine in OVA-provoked AR mice. The consequences of control, DEX, and 50 mg/kg of arbutin-supplemented AR mice were found comparable with each other [Figure 2].

Effect of arbutin on the status of malondialdehyde in the allergic rhinitis mice

As shown in Figure 3, the status of MDA was found higher in the OVA-challenged AR mice. Untreated control animals proved the normal levels of MDA. The supplementation to the OVA-provoked AR mice by the arbutin (25 and 50 mg/kg) revealed a significant reduction in the status of MDA. The 50 mg/kg of arbutin effectively abridged the MDA level than the 25 mg/kg of arbutin [Figure 3]. The results of control, DEX, and 50 mg/kg of arbutin treatment were found alike with each other.

Effect of arbutin on the levels of NF-κBp65/IκBα signaling molecules

The levels of NF-κBp65 and IκBα signaling molecules in the serum of experimental animals were examined, and the upshots are depicted in Figure 4. The status of NF-κBp65 was raised whereas IκBα was moderated in the serum of OVA-provoked AR mice. However, the status of p-NF-κBp65 and p-IκBα was raised in the AR mice. The status of inflammatory mediators, i.e., IL-1β and TNF-α, was also increased in the serum of AR mice. Stimulatingly, the arbutin-administered AR mice established the appreciable reduction in the status of NF-κBp65 and p-IκBα in the serum of AR mice. Further, arbutin raised the status of IκBα in the AR mice. The DEX treatment also modulated the levels of the signaling molecules in the OVA-challenged AR mice.

Effect of arbutin on the levels of STAT-3-related signaling molecules and cytokines

Figure 5 proves the effects of arbutin on the levels of STAT-3-related signaling molecules and cytokines in the serum of OVA-provoked AR mice. The status of STAT-3, phosphorylated STAT-3 (p-STAT-3), and RORc was harshly increased in the serum of OVA-challenged AR mice. Similarly, STAT-3-related cytokines, i.e., IL-17A, IL-5, and IL-6, were also amplified in the serum of AR mice. Further, AR mice showed a reduced status of IL-10, IL-12, and IFN-γ than the control [Figure 5]. The arbutin supplementation (25 and 50 mg/kg) to the OVA-provoked AR mice reverted back to the status of STAT-3-related signaling molecules and cytokines and set back to the near-normal level in the serum. The 50 mg/kg of arbutin presented the effective restoration of the cytokines level than the 25 mg/kg of arbutin. Arbutin contracted the STAT-3, p-STAT-3, and RORc status in the serum of OVA-challenged AR mice. Further, arbutin reduced the IL-17A, IL-5, and IL-6 and raised the status of IL-10, IL-12, and IFN-γ in the AR mice. DEX treatment

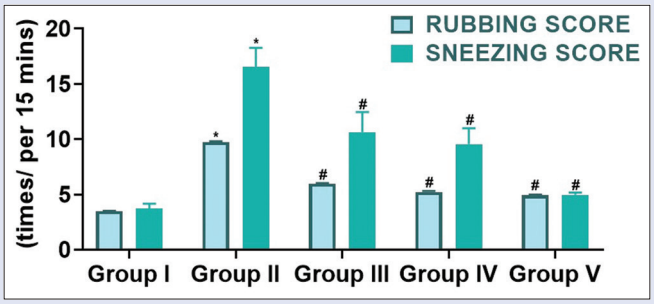

Figure 1: Effect of arbutin on the nasal symptoms of OVA-provoked AR in mice. The arbutin (25 and 50 mg/kg) supplementation to the OVA-challenged AR mice demonstrated the decreased numbers of sneezing and nasal rubbing. Results were displayed as mean ± SD of triplicates. The one-way ANOVA afterward DMRT study was executed to determine the significance level; $^{*}P < 0.05$ when related with control and $^{\#}P < 0.05$ when related with OVA-group. Group I: control; Group II: OVA-provoked AR animals; Groups III and IV: AR with 25 and 50 mg/kg of arbutin treatment, respectively; and Group V: 2.5 mg of standard drug dexamethasone-treated AR animals. AR: Allergic rhinitis; OVA: Ovalbumin; SD: Standard deviation

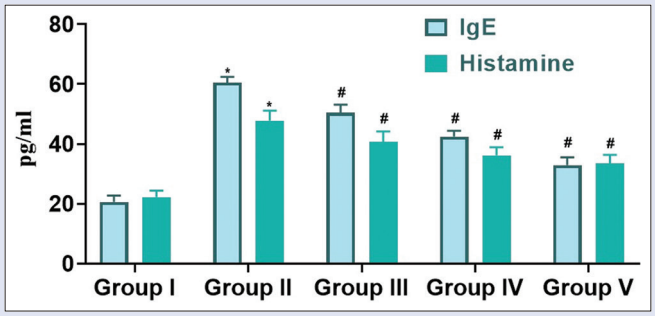

Figure 2: Effect of arbutin on the levels of OVA-specific IgE and histamine in the serum of AR mice. The arbutin (25 and 50 mg/kg) supplementation appreciably diminished the OVA-specific IgE and histamine in the serum of OVA-challenged AR mice. Results were displayed as mean ± SD of triplicates. The one-way ANOVA afterward DMRT study was executed to determine the significance level; $^{*}P < 0.05$ when related with control and $^{\#}P < 0.05$ when related with OVA-group. Group I: control, Group II: OVA-provoked AR animals, Groups III and IV: AR with 25 and 50 mg/kg of arbutin treatment, respectively and Group V: 2.5 mg of standard drug dexamethasone-treated AR animals. AR: Allergic rhinitis; OVA: Ovalbumin; IgE: Immunoglobulin E; SD: Standard deviation

also modulated the levels of signaling molecules and cytokines in the OVA-challenged mice [Figure 5].

Effect of arbutin on the histological scores

As verified in Figure 6, the histology of the nasal mucosal tissues was found normal with any variations in the control group. However, the OVA-provoked AR mice showed drastic histological adjustments such as vascular congestion, loss of ciliary, augmented goblet cells, and penetration of inflammatory cells. These signs evinced the OVA-provoked damages to the nasal mucosa. Contrastingly, arbutin (25 and 50 mg/kg) supplementation to the AR mice displayed the considerable amelioration of the ciliary loss, vascular congestion, and penetration of eosinophils [Figure 6]. The DEX administration also prohibited the nasal mucosa tissues from the OVA-provoked damages. The histological scores were found alike with the control, DEX, and 50 mg/kg of arbutin-treated AR mice.

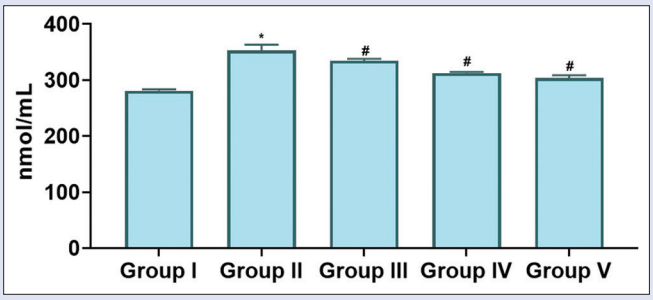

Figure 3: Effect of arbutin on the MDA level in the OVA-provoked AR in mice. The level of MDA was markedly diminished by the arbutin (25 and 50 mg/kg) supplementation to the OVA-challenged AR mice. Results were displayed as mean ± SD of triplicates. The one-way ANOVA afterward DMRT study was executed to determine the significance level; $^{*}P < 0.05$ when related with control and $^{\#}P < 0.05$ when related with OVA group. Group I: control; Group II: OVA-provoked AR animals; Group III and IV: AR with 25 and 50 mg/kg of arbutin treatment, respectively; and Group V: 2.5 mg of standard drug dexamethasone-treated AR animals. AR: Allergic rhinitis; OVA: Ovalbumin; SD: Standard deviation; MDA: Malondialdehyde

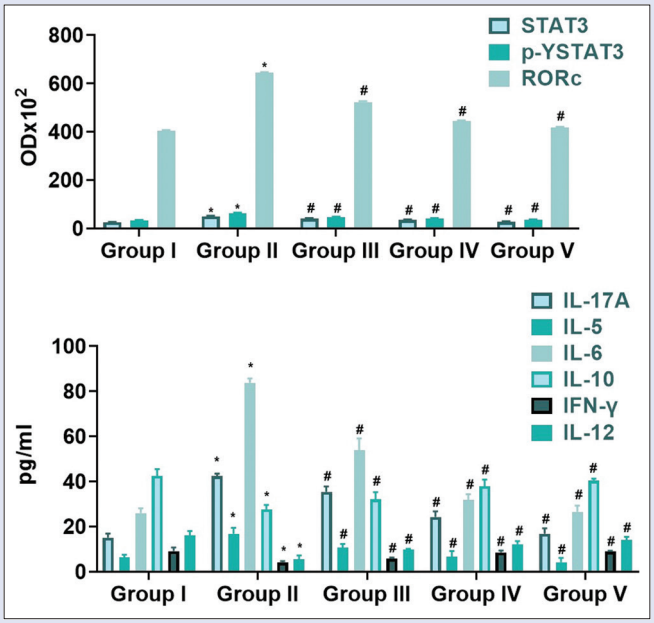

Figure 5: Effect of arbutin on the STAT3 signaling-related cytokines. The arbutin (25 and 50 mg/kg) supplementation remarkably modulated the STAT3 signaling-related cytokines in the OVA-provoked AR in mice. Results were displayed as mean ± SD of triplicates. The one-way ANOVA afterward DMRT study was executed to determine the significance level; $^{*}P < 0.05$ when related with control and $^{\#}P < 0.05$ when related with OVA group. Group I: control; Group II: OVA-provoked AR animals; Groups III and IV: AR with 25 and 50 mg/kg of arbutin treatment, respectively; and Group V: 2.5 mg of standard drug dexamethasone-treated AR animals. AR: Allergic rhinitis; OVA: Ovalbumin; SD: Standard deviation

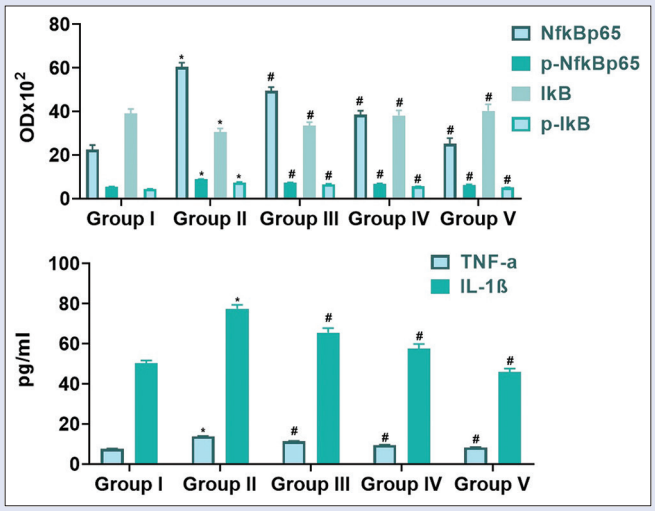

Figure 4: Effect of arbutin on the NF-κBp65/IκBα signaling-related cytokines. The arbutin (25 and 50 mg/kg) supplementation remarkably modulated the NF-κBp65/IκBα signaling-related cytokines in the OVA-provoked AR in mice. Results were displayed as mean ± SD of triplicates. The one-way ANOVA afterward DMRT study was executed to determine the significance level; $^{*}P < 0.05$ when related with control and $^{\#}P < 0.05$ when related with OVA group. Group I: control; Group II: OVA-provoked AR animals; Groups III and IV: AR with 25 and 50 mg/kg of arbutin treatment, respectively; and Group V: 2.5 mg of standard drug dexamethasone-treated AR animals. AR: Allergic rhinitis; OVA: Ovalbumin; SD: Standard deviation

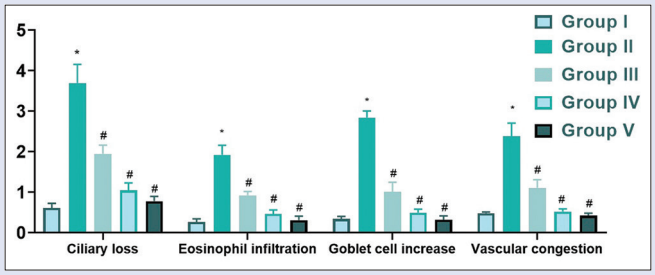

Figure 6: Effect of arbutin on the histological scores of the OVA-challenged RA in mice. The mean histological scores of the OVA-provoked AR in mice was appreciably ameliorated by the arbutin (25 and 50 mg/kg) supplementation. Results were displayed as mean ± SD of triplicates. The one-way ANOVA afterward DMRT study was executed to determine the significance level; $^{*}P < 0.05$ when related with control and $^{\#}P < 0.05$ when related with OVA-group. Group I: control; Group II: OVA-provoked AR animals; Groups III and IV: AR with 25 and 50 mg/kg of arbutin treatment, respectively; and Group V: 2.5 mg of standard drug dexamethasone-treated AR animals. AR: Allergic rhinitis; OVA: Ovalbumin; SD: Standard deviation

DISCUSSION

AR is deliberated as an utmost prime inflammatory disorder in the nasal mucosa, and the inflammation shows a key function in the instigation and progression of AR. AR declines the life quality, sleep, and performance of the patients. It was stated that AR affects nearly 40% of populations worldwide, and it continued in an increasing manner.[23] When compared with other inflammatory diseases, AR did not seem to be life-threatening, but it is a most challenging dice.[24] Allergy is an immune-regulated condition that largely caused by IgE-dependent immune reactions against the allergen. Based on the sites of allergen contact, numerous clinical appearances are illustrious by the existence of IL-4, IL-5, IL-13, and IL-17A.[25,26] In most occurrences, AR respond to the presently prevailing medications such as intranasal steroids, antihistamines, antileukotrienes, mast cell stabilizers, and corticosteroids. However, these drugs could only improve the symptoms of AR and did not give a thorough remedy in the early and late phase of AR. Further, they are often stated with more adverse effects.[27] Chlorpheniramine, diphenhydramine, and brompheniramine are the frequently recommended first-line antihistamines, which have poor selectivity, and it might produce plentiful undesirable effects such as vision blurring, tachycardia, mucous membrane drying, constipation, sedation, and urinary retention.[28] Hence, the need for the investigation of novel sources for the potent anti-inflammatory agents to treat the AR has occurred.

The initial-stage reactions of AR take place within minutes of allergen acquaintance. The histamine generation further aggravates the signs of early phase such as itching, running nose, rubbing, and sneezing.[1] Similarly, in this work, we detected that the occurrences of nasal rubbing and sneezing were raised in the OVA-provoked AR mice. Fascinatingly, the arbutin-supplemented animals presented the lessened incidences of nasal rubbings and sneezing. This result evidenced that the arbutin was upgraded to the early-phase signs of AR in mice.

Moreover, the late-phase reactions take place within the 3–9 h after the allergen exposure and are illustrious via an accretion of eosinophil in the nasal cavity. The eosinophil's resultant regulators further aggravate the epithelial injury and lead to the swelling of the nasal mucosa.[29] Inflammatory regulators such as TNF-α, IL-6, IL-10, IL-5, IL-13, and IL-17 were known to be increased during the AR progression.[30] Consequently, the tactics to prevent/reduce the status of inflammatory mediators during the progression of AR could be an auspicious target to treat the AR. The IL-4 and IL-5 boost the differentiation of Th2 cells, stimulate IgE generation from the B cells, and trigger the eosinophils; however, the IL-10 activates the differentiation of Treg cells and inhibits the stimulation of Th2 cells and IgE production.[31,32]

The NF-κB/IκB signaling cascade is contributed to the pathological progression of inflammatory disorders. The preceding reports underlined that triggering of cells with IL-1β and/or TNF-α leads to the reflective conformational switch of the NF-κB subunit p65.[33] TNF-α plays a vital function in acute and chronic inflammation. It activates the expression of plentiful immune and inflammatory regulators. TNF-α delivered by the mast cells leads to the enlarged vascular permeability and swelling of tissues. TNF-α is the foremost target for the amelioration of inflammation.[34] TNF-α could generate the stimulation of NF-κB and IκB phosphorylation.[35] In accordance with these statements, our verdicts also confirmed that the status of TNF-α and IL-1β was found increased in OVA-challenged animals with the raised NF-κBp65 and p-IκB levels. Contrastingly, the arbutin-supplemented animals verified the attenuation in the NF-κBp65, TNF-α, and IL-1β status in the OVA-provoked AR animals.

Similarly, it was stated that the STAT-3 in the T cells is indispensable for the progression of allergic inflammation. STA-3 is stimulated during the differentiation of T cells, and the presence of stimulated STAT-3 enhances the generation of Th2 cytokines.[36] In most of the cells, STAT-3 lies latent in the cytoplasm. Once it gets stirred, STAT-3 translocates to the nucleus and provokes the expression of inflammatory cytokines such as IL-6.[37] Moreover, STAT-3 and RORc are basically needed for the Th17 cells' differentiation.[38] In this study, we found that the status of STAT-3, p-STAT-3, and RORc was extremely enlarged in the serum of OVA-challenged AR mice. Further, the STAT-3-related cytokines, i.e., IL-17A, IL-5, and IL-6, were also elevated in the serum of AR mice. Captivatingly, the arbutin-supplemented AR mice relapsed back to the status of STAT-3-related signaling molecules and cytokines.

Besides, the IL-6 and IL-10 engage receptors, which could activate the STAT-3 transcription factors.[39] IL-6 further fallouts in the stimulation of the phosphorylation of STAT-3.[40] Meantime, the reduction of the IL-10 generation is because of reduced stimulation of STAT-3.[41] It was also underscored that the STAT-3 is a decisive barrier for the downregulation of Th1 reactions such as IL-12 and IFN-γ.[42] We also perceived that the AR mice showed a diminished status of IL-10, IL-12, and IFN-γ than the control. The arbutin supplementation declined the IL-17A, IL-5, and IL-6 and raised the levels of IL-10, IL-12, and IFN-γ in the AR mice. The penetration of eosinophils, vascular congestion, and loss of ciliary, augmented goblet cells are the bossy events of the AR. The chemoattractants generated by T cells, mast cells, and epithelial cells recruit the eosinophil to the mucosa.[43] In this study, we observed that the arbutin supplementation noticeably upgraded the ciliary loss, vascular congestion, and penetration of eosinophils in the AR mice.

CONCLUSION

Our verdicts confirmed that the arbutin treatment effectively ameliorated the OVA-provoked RA in mice through the modulation of inflammation. Arbutin noticeably weakened the nasal symptoms, OVA-specific IgE, and histamine in the AR mice. The arbutin treatment efficiently suppressed the levels of NF-κB/IκB and STAT-3 signaling molecules and its related cytokines. These outcomes realistically demonstrated anti-inflammatory potential of arbutin against the OVA-challenged RA in mice, and it could be auspicious therapeutic agent to treat the RA in the future.

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Conflicts of interest

There are no conflicts of interest.

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