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# QUERCETIN, LACTOBACILLUS, VITAMIN D3 – THE GOLDEN THREE THAT WILL HELP YOU WITH YOUR ALLERGY PROBLEMS

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**ABSTRACT**

**Objective:** Allergic diseases, including asthma, atopic dermatitis (AD) and allergic rhinitis (AR), are increasingly prevalent and significantly impact quality of life. These conditions are driven by an overactive Th2 immune response, leading to chronic inflammation. There is growing interest in novel therapies, such as quercetin, Lactobacillus species and vitamin $D_3$, which exhibit immunomodulatory properties and could offer new therapeutic strategies for managing allergic diseases.
**Methods:** This review explores the role of quercetin, Lactobacillus spp. and vitamin $D_3$ in modulating immune responses associated with asthma, atopic dermatitis and allergic rhinitis. We examined current literature on their mechanisms of action, effects on immune modulation and clinical evidence supporting their use in allergic conditions.
**Key findings:** Quercetin demonstrated anti-inflammatory, antioxidant, and immunomodulatory effects, reducing Th2 cytokine production and mitigating inflammation in asthma, atopic dermatitis and allergic rhinitis. Lactobacillus species, especially L. rhamnosus and L. plantarum, promoted immune tolerance by enhancing regulatory T cell activity and improving gut barrier integrity. Vitamin $D_3$, through its active form calcitriol, attenuated Th2-driven inflammation, strengthened epithelial barriers, and improved clinical outcomes in asthma, atopic dermatitis and allergic rhinitis.
**Conclusions:** Quercetin, Lactobacillus spp. and vitamin $D_3$ show promising potential as adjunctive therapies in allergic diseases. These interventions modulate key immune pathways, reduce inflammation and restore immune balance. However, further research is needed to establish optimal dosages and treatment regimens.

**KEYWORDS**

Asthma, Atopic dermatitis, Allergic Rhinitis, Immunomodulation, Epithelial Barrier, Adjunctive Therapy

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## Introduction.

Allergy is a hypersensitivity reaction triggered by immunological mechanisms. Common allergic diseases include asthma, allergic rhinitis, atopic dermatitis, all of which can significantly affect daily functioning. Symptoms may vary in severity and can appear suddenly, often exacerbated by cofactors. Allergic rhinitis (AR) affects approximately 500 million people globally and asthma impacts about 300 million. Both conditions are on the rise in prevalence, with asthma-related mortality being more common in low- and middle-income countries (Wang et al., 2023). Atopic dermatitis (AD) has a global prevalence of 8% and its lifetime prevalence reaches up to 20% (Bylund et al., 2020). In 2019, 171.17 million people worldwide were affected by AD (Dong et al., 2021). This widespread impact underscores the importance of finding additional treatment options for allergic conditions. Quercetin, *Lactobacillus* spp. and vitamin $D_3$ represent promising supportive options that could complement pharmacological therapy by reducing drug requirements and mitigating side effects. Quercetin, due to its anti-inflammatory, antioxidant and immunomodulatory properties, may act at the molecular level by inhibiting several inflammatory pathways associated with allergic reactions (Dong et al., 2021, Jerzynska et al. 2016). *Lactobacillus* spp., through modulation of the gut microbiota and enhancement of the intestinal barrier, supports immune homeostasis by limiting the excessive Th2 response characteristic of allergic diseases (Eslami et al. 2020). Vitamin $D_3$, as a regulator of immune responses, influences T lymphocyte activity, attenuating excessive inflammatory activation and improving epithelial barrier integrity, which may result in the alleviation of allergic disease symptoms (Mirzakhani et al. 2014). Through these mechanisms, therapy based on quercetin, *Lactobacillus* spp. and vitamin $D_3$ may support the treatment of allergic diseases, offering benefits such as reduced need for immunosuppressive drugs, improved patient quality of life and minimization of the risk of adverse effects associated with long-term use of conventional pharmacological therapies.

**Methodology**

This narrative review was conducted by systematically examining published literature on the roles of quercetin, *Lactobacillus* species, and vitamin $D_3$ in the management of allergic diseases, including asthma, atopic dermatitis (AD) and allergic rhinitis (AR). Relevant scientific articles were identified through searches in electronic databases such as PubMed, Scopus and Google Scholar, using keywords including "quercetin," "*Lactobacillus spp.*," "vitamin $D_3$," "asthma," "atopic dermatitis," "allergic rhinitis," "immunomodulation," and "epithelial barrier." The inclusion criteria focused on peer-reviewed studies published in English between 2000 and 2024, comprising in vitro experiments, animal studies, clinical trials, and systematic reviews that examined the therapeutic potential and mechanisms of the selected agents in allergic diseases. The extracted data were analyzed to synthesize current evidence on the immunomodulatory effects, biological mechanisms and potential clinical applications of these compounds in allergic conditions.

**Description of the State of Knowledge**

Allergic diseases exhibit different clinical and pathological features depending on the affected tissue. In allergic rhinitis (AR), exposure to aeroallergens such as dust mites, cockroach antigens, pet dander and pollens triggers inflammation in the nasal mucosa. This response involves mast cell degranulation, cytokine release (IL-3, IL-4, IL-5, IL-13) and IgE production, which contributes to the hallmark symptoms like itching, nasal congestion and rhinorrhea (Zoabi et al. 2022). Similarly, allergic asthma (AAS) shares a Th2-driven inflammatory profile, including eosinophilic and mast cell infiltration. Both AR and AAS can involve airway remodeling, leading to airway narrowing and mucus overproduction (Fahy et. Al. 2015). The pathophysiology of atopic dermatitis (AD) is more complex, involving epidermal barrier dysfunction and altered cutaneous immunity, primarily driven by type 2 T cells (Feld et al., 2016, Wolf et al., 2012).

**Mechanisms and Causes**

Allergic diseases arise from a combination of environmental and endogenous factors. Environmental triggers include altered gut microbiota, exposure to pollutants and xenobiotics, which influence immune responses (Murrison et al., (2019). Endogenous factors such as genetic and epigenetic modifications also play a significant role. Key genetic loci associated with allergic diseases have been identified, involving processes like epithelial barrier function and IgE-mediated hypersensitivity (Potaczek et al., 2017). Additionally, intracellular signaling pathways like Notch, JAK/STAT, NF-κB/MAPK and mTOR are crucial for immune regulation in allergic diseases (Wang et al., 2023). The interplay of these factors contributes to the development and persistence of allergic diseases, which can vary depending on the individual's genetic predisposition and environmental exposures.

**Quercetin and its Role in Allergic Diseases**

Quercetin (3,3′,4′,5,7-pentahydroxyflavone) is a widely studied bioactive flavonoid present in various foods, such as onions, apples and berries. Its therapeutic potential is attributed to its antioxidant, anti-inflammatory and immunomodulatory effects, making it a promising candidate for managing allergic diseases. Quercetin is known to reduce oxidative stress, a hallmark of many allergic conditions, including asthma, atopic dermatitis (AD) and allergic rhinitis (AR) (Andres et al., 2018, Li et al., 2016).

**Mechanisms of Action**

Quercetin's effects are mediated through multiple cellular processes. It regulates cytokine production, influences cell cycle progression and affects cellular energy metabolism. Additionally, quercetin modulates ion channel activity and can induce epigenetic changes, contributing to its anti-inflammatory profile (Zhu et al., 2025). It exerts its effects by influencing several key signaling pathways, including the NF-κB, MAPK and JAK/STAT pathways, which are central to immune responses and inflammation (Asgharian et al., 2022).

**Quercetin in Asthma**

In asthma, quercetin has demonstrated anti-inflammatory properties by inhibiting the release of pro-inflammatory cytokines such as TNF-α, IL-1β and IL-6. These cytokines play a crucial role in airway inflammation and quercetin reduces their production in response to allergen stimulation, thereby alleviating asthma symptoms (Rajizadeh et al., 2023). Additionally, quercetin modulates immune cell activity by inhibiting mast cell degranulation and eosinophil migration, both of which are critical to asthma pathogenesis.

Its antioxidant properties also help counteract oxidative stress, which contributes to tissue damage in the airways (Mlcek et al., 2016, Rajizadeh et al., 2023)

**Quercetin in Atopic Dermatitis**

In atopic dermatitis (AD), quercetin exerts a dual effect by modulating both inflammation and oxidative stress. Studies have shown that quercetin reduces the expression of pro-inflammatory cytokines like IL-1β, IL-6 and IL-8, while enhancing the production of anti-inflammatory cytokines such as IL-10. Additionally, it upregulates antioxidant enzymes like superoxide dismutase and catalase, providing protection against the oxidative stress commonly seen in AD. Quercetin also improves skin regeneration by inducing epithelial–mesenchymal transition (EMT) and enhancing skin barrier integrity, which is often compromised in AD (Karuppagounder et al., 2016, Beken et al. 2020).

**Quercetin in Allergic Rhinitis**

In allergic rhinitis, quercetin alleviates symptoms by modulating several inflammatory pathways. It reduces the release of cytokines like TNF-α, IL-6 and IL-4, which are involved in the allergic response and inflammation in the nasal mucosa. Quercetin also inhibits mast cell activation, thereby preventing histamine release, which is responsible for nasal congestion and itching (Naso et al., 2025).

Moreover, quercetin helps regulate the Th2-driven immune response in allergic rhinitis by modulating the production of IL-4, IL-5, and IL-13, which are key cytokines involved in IgE production and mast cell activation **(Ke et al., 2023).** By stabilizing the epithelial barrier in the nasal mucosa, quercetin reduces the susceptibility to allergen exposure and contributes to better management of the disease (Otaki et al., 2023)

**The role of quercitine**

Quercetin's multifaceted biological activities, including its anti-inflammatory, antioxidant and immunomodulatory effects, position it as a potential therapeutic agent for allergic diseases such as asthma, atopic dermatitis and allergic rhinitis. Its ability to modulate key cellular pathways and protein targets involved in inflammation and immune responses offers a promising avenue for the development of novel treatments for these chronic conditions.

**Lactobacillus species in Allergic Diseases**

Allergic diseases such as allergic rhinitis (AR), asthma and atopic dermatitis (AD) are associated with an overactive Th2-skewed immune response. This immune dysregulation is characterized by elevated levels of immunoglobulin E (IgE), eosinophilic inflammation and impaired epithelial barrier function. These conditions involve complex immune pathways, with the gut microbiota emerging as a key modulator of immune responses. Recent research suggests that probiotics, particularly Lactobacillus species, may help to restore immune homeostasis and prevent allergic reactions by modulating the gut–immune axis (Steiner, et al., 2021).

**Immunomodulatory Effects of Lactobacillus Species**

Lactobacillus species are recognized for their immunomodulatory effects, which influence both local and systemic immune responses. These probiotics help enhance the integrity of the gut epithelial barrier, stimulate mucosal immunity and reduce systemic inflammation. Lactobacillus spp. promote the generation of regulatory T cells (Tregs) and the production of anti-inflammatory cytokines, such as IL-10, which counterbalance Th2-driven inflammation seen in allergic diseases (Yuksel et al., 2023).

Moreover, Lactobacillus strains inhibit dendritic cell maturation and reduce the expression of proinflammatory cytokines and costimulatory molecules, thereby limiting allergen-induced T-cell activation (Mårtensson et al., 2022). This process is particularly important in food allergies and allergic rhinitis (AR), where immune tolerance needs to be re-established. Strains such as *Lactobacillus rhamnosus* GG and *Lactobacillus casei* have been shown to decrease clinical symptoms of allergies by modulating both local and systemic immune responses (Steiner et al., 2021).

**Metabolic Reprogramming and Barrier Integrity**

In addition to their immune-modulatory effects, Lactobacillus species contribute to the metabolic reprogramming of the host immune system. Through the production of short-chain fatty acids (SCFAs), Lactobacillus spp. promote an anti-inflammatory immune response and enhance the integrity of the epithelial barrier. These changes reduce allergen penetration and help prevent systemic sensitization (Liu et al., 2023). Lactobacillus strains contribute to maintaining gut health by reinforcing tight junctions between epithelial cells, thereby limiting endotoxin translocation and inflammation (Cui et al., 2017).

**Lactobacillus in Asthma**

Asthma is a chronic inflammatory condition of the airways, with Th2-driven inflammation playing a central role. Probiotic supplementation, particularly with Lactobacillus species, has been shown to reduce asthma-related inflammation by modulating immune responses. For example, *Lactobacillus rhamnosus* GG (LGG) promotes the expansion of Tregs and enhances the production of anti-inflammatory cytokines, which help reduce Th2-driven inflammation in asthma. In murine models of asthma, LGG has been shown to reduce airway inflammation by modulating dendritic cell maturation and influencing the Th1/Th2 balance (Feleszko et al., 2007). Furthermore, Lactobacillus supplementation improves gut barrier integrity, preventing the entry of allergens and endotoxins into the bloodstream, which is particularly beneficial in asthma (Spacowa et al., 2020).

**Gut-Lung Axis in Asthma**

The gut-lung axis plays a critical role in asthma pathogenesis. Lactobacillus probiotics can modulate the gut microbiota, which in turn influences systemic immunity. By improving gut health, these probiotics help reduce airway inflammation and eosinophilic infiltration in the lungs, leading to improved asthma symptoms. Studies indicate that children with asthma who receive Lactobacillus probiotics show reduced airway hyperreactivity and better pulmonary function (Huang et al., 2018).

**Lactobacillus in Atopic Dermatitis**

Atopic dermatitis (AD), characterized by chronic inflammation of the skin, can benefit from Lactobacillus-based interventions. Lactobacillus species have shown beneficial effects in AD by promoting immune homeostasis and enhancing skin barrier function. For instance, *Lactobacillus plantarum* CJLP133 has been shown to downregulate Th2 cytokines (e.g., IL-4, IL-5) while promoting Th1 responses, thus contributing to immune balance in AD patients (Han et al., 2012).

*Lactobacillus rhamnosus* GG (LGG) has been demonstrated to improve gut barrier function and mitigating skin inflammation (Fu et al., 2019). Furthermore, specific strains like *Lactobacillus paracasei* KBL382 promote the expansion of Tregs, crucial for maintaining immune tolerance and controlling excessive inflammatory responses in AD (Kim et al., 2020).

**Conclusion about Lactobacillus species**

Lactobacillus species offer considerable promise in managing allergic diseases, including allergic rhinitis, asthma and atopic dermatitis. Through immunomodulation, reinforcement of epithelial barriers and promotion of immune tolerance, Lactobacillus probiotics can play a key role in reducing allergic inflammation and improving patient outcomes. However, further research is needed to determine the optimal strains, dosages, and treatment durations for probiotic therapy in these diseases.

**Vitamin $D_3$ in Allergic Diseases: A Mechanistic Overview**

**Introduction**

Vitamin $D_3$ (cholecalciferol) is a fat-soluble vitamin with well-documented roles in bone health, but emerging evidence has highlighted its significant immunomodulatory properties. The active form of vitamin $D_3$, 1,25-dihydroxyvitamin $D_3$ (calcitriol), exerts broad effects on both innate and adaptive immune responses. Particularly in the context of allergic diseases such as asthma, atopic dermatitis (AD), and allergic rhinitis (AR), vitamin $D_3$ plays a crucial role in modulating immune pathways that contribute to disease pathogenesis (Searing et al., 2010).

**Vitamin $D_3$ and Asthma**

Asthma is a chronic inflammatory disorder characterized by airway hyperresponsiveness and obstruction, largely driven by an exaggerated T helper type 2 (Th2)-mediated immune response. Th2 cytokines such as IL-4, IL-5 and IL-13 promote inflammation and IgE production, which are hallmark features of asthma. Vitamin $D_3$ through its active form calcitriol, influences asthma pathogenesis via the vitamin D receptor (VDR), present on various immune cells, including T and B lymphocytes, macrophages and dendritic cells (Pfeffer et al., 2018).

Several studies suggest that vitamin $D_3$ supplementation can attenuate Th2-driven inflammation by inhibiting Th2 cell proliferation and reducing cytokine production, particularly IL-4 and IL-13 (Lange et al., 2009). Moreover, vitamin $D_3$ promotes the differentiation of regulatory T cells (Tregs), which are essential for immune tolerance and suppression of excessive inflammatory responses (Bock et al., 2011). Deficiency in vitamin $D_3$ has been linked to increased asthma severity, frequent exacerbations and diminished lung function (Liu et al., 2019). Furthermore, vitamin $D_3$ enhances airway epithelial integrity by upregulating proteins such as E-cadherin, which are crucial for maintaining the barrier function of the airway epithelium and preventing inflammatory cell infiltration (Rybakovsky et al., 2023).

**Vitamin $D_3$ and Atopic Dermatitis**

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease, characterized by pruritic egzematous lesions and defective skin barrier function. Similar to asthma, AD is associated with a skewed Th2 response, characterized by the production of IL-4, IL-5 and IL-13, leading to increased IgE synthesis and eosinophilic inflammation. In this context, vitamin $D_3$ plays a dual role in modulating both immune responses and skin barrier function.

Vitamin $D_3$, through calcitriol binding to the VDR in keratinocytes and immune cells, regulates immune responses by inhibiting the production of Th2 cytokines, thereby alleviating inflammatory skin reactions (Umar et al. 2018). Additionally, vitamin $D_3$ enhances the expression of antimicrobial peptides such as cathelicidin (LL-37), which are often deficient in AD patients and contribute to the skin's susceptibility to infections (Reinholz et al., 2012). In terms of barrier function, vitamin $D_3$ promotes the expression of structural proteins such as filaggrin, which is critical for maintaining skin hydration and preventing allergen penetration (Umehara et al. 2023). Clinical studies have demonstrated that vitamin $D_3$ supplementation can also reduce disease severity (Imoto et al. 2021).

**Vitamin $D_3$ and Allergic Rhinitis**

Symptomatic improvement following Vitamin D3 supplementation in patients with allergic rhinitis may be attributed to its immunomodulatory properties, as it influences both the innate and adaptive immune systems. Vitamin D regulates the functions of T cells, B cells, dendritic cells, monocytes and macrophages. It inhibits T cell proliferation, induces a shift from a TH1 to a TH2 immune response and promotes the production of regulatory T cells, which play a crucial role in the course of allergic rhinitis. Additionally, Vitamin D triggers apoptosis of activated B cells while suppressing their differentiation into plasma cells and the secretion of immunoglobulins, including IgE. Therefore, Vitamin D may act as a disease modulator, improving the quality of life in individuals with allergic rhinitis (Kalsotra et al., 2022).

Moreover, vitamin $D_3$ plays a role in enhancing the epithelial barrier function in the upper airways. Studies on human sinonasal epithelial cells have shown that vitamin $D_3$ upregulates the expression of tight junction proteins such as occludin and claudins, thereby reinforcing mucosal integrity and reducing allergen permeability. This helps prevent immune activation and attenuates the inflammatory cascade characteristic of allergic rhinitis (Ma et al., 2020).

**Conclusions about Vitamin D**

Vitamin $D_3$ is a key regulator of immune responses in allergic diseases. Its immunomodulatory effects, including the suppression of Th2-driven inflammation, enhancement of Treg function and improvement of epithelial barrier integrity, make it a promising adjunctive therapy in asthma, atopic dermatitis and allergic rhinitis. While clinical evidence supports the beneficial role of vitamin $D_3$ supplementation, further studies are needed to determine optimal dosages, treatment durations and patient populations that would benefit most from vitamin $D_3$ intervention.

**Discussion**

The findings presented in this review highlight the promising role of quercetin, *Lactobacillus* species and vitamin $D_3$ as adjunctive interventions in the management of allergic diseases such as asthma, atopic dermatitis (AD) and allergic rhinitis (AR). Each of these compounds exhibits immunomodulatory properties that target different aspects of allergic inflammation, offering a multi-faceted approach to treatment beyond conventional pharmacotherapy.

Quercetin's ability to inhibit key inflammatory pathways (e.g., NF-κB, JAK/STAT, MAPK) and reduce Th2 cytokine production demonstrates its relevance in suppressing allergic responses across various tissues. By mitigating oxidative stress and stabilizing mast cells, quercetin contributes to the attenuation of symptoms and may reduce reliance on corticosteroids and antihistamines.

*Lactobacillus* species, particularly *L. rhamnosus* and *L. plantarum*, influence both local and systemic immunity by enhancing regulatory T cell activity, promoting anti-inflammatory cytokines such as IL-10 and improving epithelial barrier function. Their impact on the gut-lung and gut-skin axes highlights the central role of the microbiome in allergic disease modulation. The observed improvements in disease markers and clinical outcomes suggest that probiotic supplementation could offer a preventive and therapeutic benefit, especially in early-life interventions.

Vitamin $D_3$ through its active form calcitriol, plays a pivotal role in downregulating Th2-driven inflammation and enhancing epithelial integrity across respiratory and cutaneous tissues. Its ability to increase regulatory T cell activity, promote antimicrobial peptide expression and upregulate tight junction proteins underlines its broad systemic benefits. Notably, vitamin $D_3$ deficiency has been associated with worse outcomes in allergic diseases, indicating the importance of adequate levels for disease control.

The implications of these findings are significant. They point toward a shift in allergic disease management strategies—from solely suppressing symptoms to restoring immune balance and barrier integrity. However, despite encouraging evidence, the clinical application of these agents remains constrained by variability in dosage, bioavailability and treatment duration across studies. Further well-designed, large-scale randomized controlled trials are essential to establish standardized protocols and to determine their long-term safety and efficacy in diverse populations.

**Table 1.** Comparison of the Immunomodulatory Effects of Quercetin, Lactobacillus spp., and Vitamin $D_3$ in Allergic Diseases

| Substance | Main Mechanisms of Action | Effects on Immune System | Clinical Impact (AR, AD, Asthma) |
|---|---|---|---|
| **Quercetin** | • Inhibition of mast cell degranulation<br>• Reduction of Th2 cytokines (IL-4, IL-5, IL-13)<br>• Antioxidant activity | • Decreased inflammatory cell activity<br>• Modulation of NF-κB and Nrf2 pathways | •Alleviation of asthma and allergic rhinitis symptoms<br>• Improvement of skin condition in AD |
| **Lactobacillus spp.** | • Enhancement of gut barrier integrity<br>• Induction of regulatory T cells (Tregs)<br>• Production of short-chain fatty acids (SCFAs) | • Restoration of Th1/Th2 balance<br>• Promotion of immune tolerance | • Reduction of AD and asthma symptoms<br>• Decreased allergic rhinitis recurrence |
| **Vitamin $D_3$** | • Activation of Vitamin D receptor (VDR)<br>• Increased expression of barrier proteins (filaggrin, E-cadherin)<br>• Induction of Tregs | • Suppression of Th2 responses<br>• Enhancement of innate immunity | • Improved respiratory function<br>• Reduced severity of AD and AR symptoms |

**Conclusions**

Quercetin, *Lactobacillus* spp. and vitamin $D_3$ show promising potential as adjunctive therapies in allergic diseases such as asthma, atopic dermatitis and allergic rhinitis. Each of these compounds exerts beneficial immunomodulatory effects by reducing inflammation, enhancing barrier function and restoring immune balance. Although current findings are encouraging, further clinical research is needed to establish optimal doses, treatment durations and combinations. Future studies should also explore personalized approaches that consider individual immune profiles and microbiota composition to improve treatment outcomes.

**Disclosure**

**Author's contribution**

Conceptualization: Barbara Pękowska, Adrianna Brzozowska, Karolina Niewczas, Katarzyna Kozon; Methodology: Barbara Pękowska, Adrianna Brzozowska, Anna Bielicka, Irmina Czerepak; Software: Michał Bzoma, Adam Niedziela, Dominik Domoń; Check: Barbara Pękowska, Karolina Jaros, Hubert Bochenek; Formal analysis: Barbara Pękowska, Katarzyna Kozon, Anna Bielicka, Julia Gugulska; Investigation: Adrianna Brzozowska, Julia Gugulska, Michał Bzoma; Resources, Data curation: Barbara Pękowska, Adrianna Brzozowska, Karolina Niewczas, Katarzyna Kozon, Anna Bielicka, Hubert Bochenek, Irmina Czerepak, Julia Gugulska, Michał Bzoma , Karolina Jaros, Adam Niedziela, Dominik Domoń; Writing-rough preparation: Barbara Pękowska, Karolina Niewczas, Anna Bielicka, Irmina Czerepak; Writing-review and editing: Adrianna Brzozowska, Katarzyna Kozon, Hubert Bochenek; Visualization: Adrianna Brzozowska, Michał Bzoma; Supervision: Barbara Pękowska, Karolina Niewczas, Karolina Jaros; Project administration: Barbara Pękowska, Adam Niedziela, Dominik Domoń.

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