

The therapeutic potential of bacterial lysates: applications and future perspectives

Potențialul terapeutic al lizatelor bacteriene: aplicații și perspective de viitor

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Rezumat

Utilizarea lizatelor bacteriene în terapie a câștigat avânt datorită capacității lor de a modula răspunsurile imune ale gazdei. Aceste preparate, derivate din liza celulelor bacteriene, conțin componente antigenice care stimulează atât imunitatea înăscută, cât și cea adaptativă. În ciuda aplicațiilor lor clinice în patologii infecțioase, alergice și oncologice, mecanismele moleculare care stau la baza eficacității lor rămân subexplorate. Acest articol trece în revistă înțelegerea actuală a lizatelor bacteriene, concentrându-se pe aplicațiile lor terapeutice și pe direcțiile viitoare de cercetare.

Abstract

The use of bacterial lysates in therapy has gained momentum due to their ability to modulate host immune responses. These preparations, derived from bacterial cell lysis, contain antigenic components that stimulate both innate and adaptive immunity. Despite their clinical applications in infectious, allergic, and oncological pathologies, the molecular mechanisms underlying their efficacy remain underexplored. This article reviews the current understanding of bacterial lysates, focusing on their therapeutic applications and future research directions.

Introduction

Bacterial lysates (BL) have emerged as immunomodulatory agents with broad applications in medicine.

Derived from the lysis of bacterial cells, these preparations contain a mixture of bacterial components, including proteins, lipopolysaccharides, and DNA, which interact with the host immune system to enhance both innate and adaptive responses.

Clinically, bacterial lysates have demonstrated effectiveness in managing infections (particularly in the respiratory

tract), improving vaccine responses, and mitigating allergic reactions.

The interaction between the immune system and microbial components has been crucial in shaping therapeutic approaches to infectious and immune-related diseases.

Despite their long-standing use, the precise mechanisms through which bacterial lysates exert their effects remain an ongoing area of research [24].

Bacterial lysates are a mixture of antigens obtained from lysed bacteria in culture, subsequently lyophilized through mechanical or chemical processes, and combined with excipients to be tabletized.

The chemical lyophilization process involves the use of alkaline pH substances, which can denature the protein fraction and reduce immunogenic capacity.

Thus, the mechanical method is preferred, as it preserves antigen structure [1].

First introduced in therapeutic protocols in the 1970s, the use of bacterial lysates brings new benefits today, demonstrating their potential as a useful alternative to antibiotics [13,22].

Studies have shown that BLs are efficient immunostimulators, triggering specific immune responses, and are therefore used preventively or curatively in various bacterial and viral infections [21].

They have been most commonly and successfully employed for respiratory tract infections and in the treatment of chronic obstructive pulmonary disease (COPD) [11,21].

In recent decades, studies investigating BLs have also highlighted their beneficial effects in preventing and treating atopic dermatitis, allergic rhinitis, and asthma in children and adults [12].

Over time, bacterial lysates have proven particularly effective in geriatric and pediatric patients. In these two patient categories, therapeutic protocols often include products based on inactivated microbial agents to enhance immune reactivity.

In children, the antibody response to viruses or bacteria is suboptimal due to an underdeveloped immune system.

Similarly, in older adults, the immune response is neither prompt, nor adequate due to a senescent immune system [1].

Currently, in the EU member states, eight drugs containing six different combinations of bacterial strain lysates are authorized for use in respiratory conditions.

These medications have different names across member states, with the most well-known being Ismigen, Broncho-Vaxom, Ribomunyl, Luivac, and Lantigen B. Typically, these products contain mixtures of

several bacterial species most frequently responsible for respiratory tract inflammation, including *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Klebsiella ozaenae*, *Haemophilus influenzae*, and others, with the composition varying by product (Fig. 1) [13].

	Ismigen	Luivac	Broncho-Vaxom	Ribomunyl
<i>Staphylococcus aureus</i>	X	X	X	–
<i>Streptococcus pneumoniae</i> Xtype 1, 2, 3, 5, 8, 47		X	X	X
<i>Streptococcus pyogenes</i>	X	X	X	X
<i>Streptococcus viridans</i>	X	<i>Streptococcus mitis</i>	X	–
<i>Moraxella catarrhalis</i>	X	X	X	–
<i>Haemophilus influenzae</i>	X	X	X	X
<i>Klebsiella pneumoniae</i>	X	X	X	X
<i>Klebsiella ozaenae</i>	X	–	X	–

Figure 1. Composition of bacterial lysates used in the prevention of respiratory tract infections.
(Source: Jurkiewicz și Zielnik-Jurkiewicz, 2018)

The aim of this short review is to provide an overview of the molecular and immunomodulatory mechanisms of bacterial lysates, their therapeutic applications, and future perspectives, highlighting their potential in personalized medicine.

Mechanism of action of bacterial lysates

The triggering of the immune response following the administration of bacterial lysates is achieved through the recognition of antigen particles by specific cellular receptors (TLR – Toll-Like Receptors),

expressed on the surface of monocyte and macrophage membranes.

These cells are then activated and induce the differentiation of DCs, resulting in the stimulation of T lymphocytes, especially T helper lymphocytes [1,19].

BLs can even activate B lymphocytes, which, through differentiation, generate specific IgA antibodies, these antibodies being the first to act against bacteria [15].

As a summary of the mechanism of action of BLs, it can be suggested that they are capable of generating responses in immunocompetent cells through direct cellular activation, stimulation of immune effector cells, or the production of cytokines and various signaling pathways [1,23].

The activation of both nonspecific and specific immunological pathways is necessary for bacterial lysates to exert their immune impact.

The activation of nonspecific mechanisms (innate immune system) involves signal transmission by TLRs (TLR-2/TLR-6, TLR-9, and TLR-7/TLR-8), an increase in chemotaxis, as well as the cytotoxic and phagocytic activity of phagocytes, an increase in natural killer cell activity, DC activation along with a proliferation of their antigen-presenting capacity, and increased migration to the respiratory tract.

The activation of specific mechanisms (acquired immune system) is marked by an increased concentration of immunoglobulins (IgA and IgG antibodies), enhanced T cell activity and the capacity to activate other specific mechanisms (activation of T and B cells), activation of B cells (CCL2, CCL3, CCL20, CCL22, BAFF, IL-6, and APRIL), and increased activity of regulatory T cells CD4⁺ CD25⁺ Foxp3⁺ [18]. (Fig. 2).

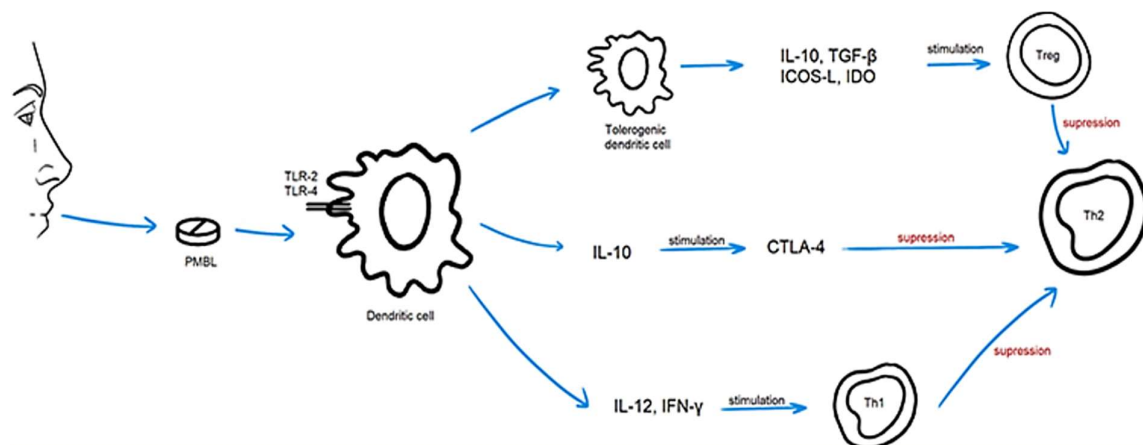


Figure 2. Mechanism of action of bacterial lysates. (Source: Janeczek și col., 2022)

In cancer therapy, the activation and stimulation of NK cells and macrophages using bacterial products have demonstrated the ability to correct the inadequacy of the immunosuppressive tumor micro-environment.

The classical activation of macrophages, which is associated with high IL-12 and low IL-10, by bacterial products can counteract the protumor effects associated with the tumor.

IL-10 effectively regulates pro-inflammatory cytokines, including IL-1, IL-6, and TNF- α , although its actions are not limited to these mediators.

In fact, IL-10 also inhibits the synthesis of chemotactic substances such as IL-8 and chemokines that can attract more leukocytes to the site of inflammation [18]. (Fig. 3)

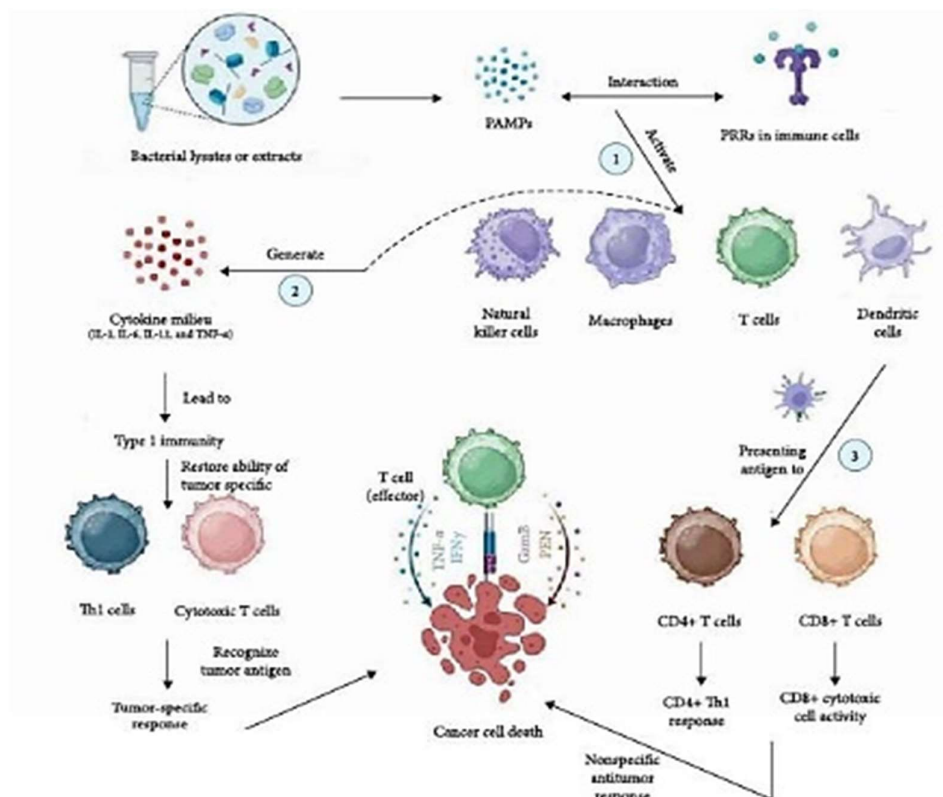


Figure 3. Mode of action of bacterial lysates in cancer immunotherapy. (Source: Rahman și col., 2024)

Clinical applications of bacterial lysates

The use of LBs in respiratory infections

The benefits and efficacy of bacterial lysates in preventing recurrent bacterial infections have been confirmed in numerous clinical studies.

The results of analyses suggest significant potential for reducing antibiotic use in recurrent respiratory tract infections, especially in children [13].

The meta-analysis conducted by Del-Rio-Navarro et al. showed that, compared to placebo, bacterial lysates reduced the incidence of respiratory tract infections by 41.21% [6].

Schaad et al. demonstrated that the effectiveness of preventing respiratory tract infections was greater with a higher incidence of infections, thus confirming

better efficacy of bacterial lysates in patients experiencing more frequent recurrences. The reduction in incidence rate was 35.5% compared to placebo [20].

Gutierrez-Tarango and Berber observed that bacterial lysates not only reduced the incidence of respiratory tract inflammations but also shortened the duration of infections and reduced the number of antibiotic courses [9,13].

Cai et al. investigated in their studies the effect of adding bacterial lysate-based products to pulmonary tuberculosis therapy.

Disease progression following *Mycobacterium tuberculosis* infection is closely associated with the host's immune response, with the vast majority of tuberculosis patients having reduced immune function.

Immunotherapies can regulate the immune system in patients with latent tuberculosis infection or active disease, resulting in better control of *Mycobacterium tuberculosis* replication.

The evidence presented in their study on the benefits of bacterial lysates in tuberculosis patients is encouraging, offering a better prognosis [4,24].

Meta-analyses conducted by Troiano et al. and Huang et al., on the use of bacterial lysates in chronic obstructive pulmonary disease (COPD), demonstrated that they significantly contributed to reducing the average number of COPD exacerbations as well as the number of days of antibiotic treatment.

Thus, bacterial lysates could help avoid the overuse of antibiotics and, implicitly, the emergence and development of antibiotic resistance [5,11,22].

The use of LBs in allergic diseases

Han et al. studied the immunomodulatory effect of certain bacterial lysates on allergic rhinitis in mice and determined that bacterial lysate-based products could represent a cheap and useful candidate for preventing allergic rhinitis [10].

Meng et al. observed that the bacterial lysate-based product OM-85 could alleviate persistent allergic rhinitis in patients by improving the Th1/Th2 cytokine balance in the nasal mucosa [17].

The results of the study conducted by Banche et al. on the use of bacterial lysates in allergic rhinitis showed a significant reduction in symptoms in the group using

bacterial lysates are being explored in neoplastic conditions due to their capacity to improve the patient's immune system and ability to respond to tumor cells, thereby limiting and preventing tumor development and spread [18].

Discussions and future perspectives

As fundamental science, technology, and clinical research advance, bacterial lysates will progressively establish themselves as innovative products for

lysates, including decreased nasal congestion, rhinorrhea, and ocular symptoms [2,14].

In 2015, Lu et al. presented the results of a study they conducted to evaluate the efficacy of bacterial lysates combined with conventional treatment for asthma in children, highlighting the effectiveness of lysates in reducing the frequency of asthma attacks [14,16].

The study conducted by Emeryk et al. also indicated a significant reduction in the frequency and duration of asthma exacerbations and the use of rescue medications in the group using bacterial lysates compared to the placebo group [8,14].

In 2017, Bodemer et al. conducted a study on the clinical efficacy of bacterial lysates in the treatment of atopic dermatitis.

Their results confirmed the efficacy of lysates, with patients in the observation group experiencing significantly fewer new eruptions [3].

The use of LBs in neoplastic diseases

Numerous studies suggest that bacterial lysates can act as adjuvants, enhancing the efficacy of antitumor vaccines.

Their ability to stimulate dendritic cells and promote cytotoxic T-cell responses makes them promising candidates for cancer immunotherapy. Several extracts containing combating cancer and other infectious diseases.

Further investigations will enable a full understanding of their mechanism of action and likely reveal how bacterial lysate immunotherapy functions, including how bacterial constituents regulate immune responses.

This will accelerate the development of more targeted and effective medications [18].

Although numerous studies have demonstrated the efficacy of bacterial

lysates in various pathologies, there is an urgent need for high-quality studies with large sample sizes regarding the clinical use of lysates with different bacterial antigen compositions.

Additionally, research is needed to explore various preparation methods, administration routes, and dosages [14].

Although in recent years there has been an increase in the frequency of clinical trials using bacterial lysates, data on their inclusion in therapeutic protocols remain limited. Nevertheless, the clinical efficacy and safety benefits of adding lysates to standard therapies are compelling reasons to continue research in this field [12].

Conclusions

Bacterial lysates consist of fragments derived from lysed bacterial cells and represent a unique class of immunostimulants capable of enhancing host immunity. Although they were initially used only in the prevention and treatment of recurrent respiratory infections, their clinical applications have expanded into allergy management and cancer immunotherapy.

The efficacy of bacterial lysates is supported by studies demonstrating their ability to activate both innate and adaptive immunity when incorporated into treatment regimens.

Bacterial lysates are versatile immunomodulators across various medical fields, from infections to cancer; however, to fully realize their potential, further research is needed to address challenges related to standardization and therapeutic application.

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