

Therapeutic Potential of Probiotics in Burn Management: Mechanisms, Clinical Applications, and Future Directions

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Abstract:

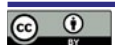
Extensive burns impair systemic homeostasis by precipitating a hyperinflammatory reaction. The dysregulation predetermines the development of complications in patients, including infections, sepsis, and metabolic disorders. Probiotics are live microorganisms that have been associated with health-promoting effects at sufficient doses, generating an increasing clinical interest in the role of probiotics during the treatment of burn-injured patients in reducing the incidence of complications and accelerating the recovery process. The current review examines the molecular and physiological mechanisms involved in the effects of probiotics on gut microbiota, host defense, inflammation, and wound healing in burn management. The findings indicate that probiotics may enhance the healing process by modulating the immune response and promoting a balanced gut microbiome. Further investigations are needed to establish standardized protocols for probiotic administration in clinical settings, ensuring optimal outcomes for patients with burn injuries. It also reviews the scientific and clinical data that supports probiotic use in infection prevention, wound repair, and systemic inflammation control. Lastly, the article explains the issues related to the clinical use of probiotic therapy and suggests future areas of research to maximize its use in burn treatments.

Keywords: Probiotics, burn management, gut microbiota, immune modulation, infection prevention.

Introduction

The growing occurrence of burns, which rank among the most devastating injuries, demands prompt action. On top of being a common cause of sickness and impairment, they endanger millions of lives every year, to varying degrees. Surface skin and tissue damage isn't the only thing burns

do; they can also trigger a cascade of other, more catastrophic complications. Burn victims have an increased risk of significant inflammation, reduced immune function, sepsis, multi-organ failure, slower wound healing, and subsequent infections. The length and severity of the burn, coupled with the body's reaction to it, considerably determine the



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prognosis and recovery process (1, 2, 3).

There are a lot of aspects that determine how the body handles burns. A skin injury damages the epidermis, the skin's protective barrier, setting off a chain reaction of inflammatory reactions and changes in the immune system. Although some degree of inflammation is normal and even expected after a small burn, it can become life-threatening in the event of a severe burn. Opportunistic infections are more common due to this disorder's inflammatory effects and immune system weakness. Additionally, systemic inflammation can cause harm to distant organs and an increased risk of mortality (4, 5).

Changes to the gut flora as a result of burns have received less focus from researchers. In terms of homeostasis and immunity, the stomach is a factor. Intestinal pathogens and their toxins can enter the bloodstream through weakened intestinal barriers caused by thermal damage. Endotoxemia and systemic inflammation could both be worsened by this. When the gut microbiota is out of whack, a condition known as dysbiosis, burn patients have a harder time recovering and have worse clinical outcomes (7). Recently, the therapeutic application of probiotics in medicine and surgery has gained increasing scientific and clinical interest. Probiotics are live microorganisms that, when consumed moderately, can benefit host health. They inhibit the growth of pathogens, maintain the gut microbial balance, and promote mucosal barrier function (9). Probiotics have immunomodulatory effects that help the body keep its inflammatory and anti-inflammatory responses in check, increase production of pro-inflammatory cytokines, and boost regulatory T cell activity. Uncontrolled inflammation and impaired immunity significantly contribute to the clinical worsening of burn patients, making these features all the more important for these patients (10).

Probiotics lessen the likelihood of burn complications, such as the fatal sepsis and pneumonia, according to animal and human research. As a result of their beneficial effects on the intestinal microbiota, probiotics reduce systemic inflammation and prevent harmful bacteria from penetrating the bloodstream. Furthermore, probiotics speed wound healing, which may be because of their effects on growth factors, angiogenesis, and epithelial remodeling, according to multiple studies (11).

According to this article, probiotics can change the microbiota, boost immunity, reduce inflammation, and help with tissue regeneration. Beyond that, it evaluates the existing clinical evidence, identifies research gaps, and proposes probiotic-enhanced future operations. The use of the microbiota in novel burn treatments is an emerging field of study,

which includes this review.

The Role of Probiotics in Rehabilitation from Burns

The gut microbiota plays a crucial role in human health by regulating inflammation, maintaining an intact intestinal barrier, and aiding in immune system homeostasis. The trillions of bacteria and other microbes that call the intestines home make up what is known as the gut microbiome, and its effects reach well beyond the digestive tract (12). In addition to strengthening the immune system, preserving the integrity of the gut's epithelial barrier, and creating important metabolites like short-chain fatty acids (SCFAs) are also vital functions performed by these microorganisms. To be healthy, one needs a diverse and balanced gut flora. The reason behind this is that it regulates the immune system's response to foreign antigens, prevents the spread of dangerous microorganisms, and keeps cytokines in balance (13).

Gut dysbiosis is a condition that can arise when the delicate microbial balance is upset. This imbalance can be triggered by burn damage. Opportunistic pathogens, particularly Enterobacteriaceae, can overwhelm beneficial commensal bacteria, such as Lactobacillus and Bifidobacterium species, leading to the development of dysbiosis (14). Reduced blood supply to the gastrointestinal tract, systemic inflammation, antibiotic use, decreased gut motility, and other factors may hasten the shift in microbial composition. A lot of people who have burns go through all of these things. Endotoxins and bacteria in the intestines are able to breach the mucosal barrier and enter the circulation because of these modifications (15).

Those who suffer from burns may be at risk for major effects if they encounter dysbiosis in their gut. Some of the potentially deadly outcomes include significant systemic inflammation, impaired immunology, delayed tissue repair, an increased risk of sepsis, and failure of multiple organs (16). The majority of secondary infections in burn patients are caused by bacterial translocation as a consequence of decreased barrier function (17). Probiotics may lessen the severity of these side effects by reestablishing a healthy balance of gut bacteria. Taking these live microbial supplements at the correct dosages can cause a number of positive changes in the gut ecology (18). In addition to creating bacteriocins and organic acids, which limit the spread of dangerous bacteria, they also encourage the growth of good bacteria while inhibiting the growth of bad bacteria. Increased levels of tight junction proteins and host defense peptides, as well as a stronger intestinal barrier, are all benefits of probiotics (19).

All aspects of the immune system are affected by probiotics because they have the ability to change the

microbiota and improve the performance of regulatory T cells simultaneously. Furthermore, they have the ability to reduce the levels of inflammatory mediators like TNF- α and IL-6, while simultaneously elevating the levels of cytokines that promote inflammation inhibition, such as IL-10. These immunological benefits are of the utmost importance since burns present a delicate and frequently dangerous balance between the suppression of the immune system and the excessive inflammation that occurs alongside it. By lowering the inflammatory cascade and boosting mucosal immunity, probiotics create an environment that is more conducive to the healing of wounds and improving the likelihood of systemic recovery (20).

To summarize, the multi-pronged approach to treating burn injuries with probiotics aims to improve clinical outcomes by restoring microbial balance, preserving the intestinal barrier, modifying the immune response, and other similar mechanisms. The rationale for this is that probiotic therapy is an excellent supplement to traditional burn care, and there is emerging evidence that it ought to be a component of future techniques that will assist burn patients in recovering more quickly and with less difficulty.

Probiotic-Induced Immune Modulation in Burn Injuries

The immune system undergoes a complex series of events over many weeks or months following burns or other traumas. Inflammation (also known as SIRS) and immunosuppression (also known as CARS) are the two phases of the illness progression (21). Opportunistic infections, sepsis (the leading cause of mortality in burn victims), significant tissue damage, and a delayed healing process are just a few of the many problems that can arise when the immune system is overactive. The dual danger of immune suppression and systemic inflammation necessitates immediate efforts to discover treatments that might normalize the immune system and strengthen the host's defenses (22).

Immunological responses in burn patients may be impacted by interactions between probiotics and gut-associated lymphoid tissue (GALT), an important node in the systemic immune regulation network (23). Intestinal epithelial cells, dendritic cells, and pattern recognition receptors such toll-like receptors (TLRs) are just a few of the cell types that probiotics can interact with once they enter the intestines. These interactions impact the innate and adaptive immune systems via the signaling pathways that they trigger or regulate (24).

By increasing the number and activity of macrophages and natural killer (NK) cells, probiotics strengthen the host's first line of defense against invaders within the framework of innate

immunity. They influence the function of antigen-presenting cells and are critical for the activation and maturation of T lymphocytes. Dendritic cells are referred to by various names. It is possible that probiotics and dendritic cells will work together to modify T cell responses in a way that is less inflammatory and more regulated (25). Researchers have found that numerous probiotics, particularly those belonging to the *Lactobacillus* and *Bifidobacterium* genera, have the ability to reduce quantities of significant pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6. This aids in the regulation of these cytokines. Increased blood levels of these cytokines after heat damage (26). An integral aspect of the body's inflammatory response system are these cytokines. They cause harm to different organs, malfunction of the endothelium, and leakage of capillaries. Intestinal inflammation is reduced by probiotics because they decrease their expression (27).

The body produces more anti-inflammatory cytokines, including transforming growth factor-beta (TGF- β) and interleukin-10 (IL-10), and regulatory T cells (Tregs), with the help of probiotics. Reducing the likelihood of collateral tissue damage while keeping the ability to resist infections is achieved by improving immunological tolerance and avoiding the over-activation of immune responses (28).

The effects of these immunomodulators go well beyond the gastrointestinal tract and have the potential to affect immune responses systemically. Since microbial substances and pro-inflammatory signals can travel through the epidermal and mucosal barriers, burn sufferers are at a higher risk of developing sepsis. The ways in which probiotics influence systemic inflammation and mucosal immunity allow them to alleviate or eliminate septic sequelae (29).

A healthy gut microbiota supports human health by reducing inflammation, preserving strong barriers, and improving immunological stability. The gut microbiota has an impact beyond digestion (12). There are billions of bacteria and other living things in this huge network. These microorganisms make short-chain fatty acids (SCFAs), which help keep the gut epithelial barrier strong and boost the immune system. A varied and balanced gut microbiota is associated with improved health. This is because it affects how the immune system reacts to foreign antigens, stops harmful pathogens from getting in, and controls the production of cytokines (13, 14).

A burn victim who develops stomach dysbiosis may experience life-threatening complications. Death can happen because of a weak immune system, a higher risk of getting infections, slow healing of tissues, or organ failure (15, 16). A lot of people who get burned end up in the hospital or die from their

injuries because of secondary infections. The main reason for these problems is that bacteria get through the body's defenses (17).

Probiotics help by bringing back a healthy balance of gut flora. When used as directed, these live microbial supplements can help the gut in many ways (18). They make organic acids and antibiotic bacteriocins, which help good bacteria and stop bad bacteria from growing. Probiotics increase levels of gut tight junction protein and host defense peptide, which strengthens the gut barrier (19).

Probiotics affect the immune system in many ways, including changing the microbiota and making regulatory T cells work harder. They also raise IL-10 levels and lower inflammatory mediators like TNF- α and IL-6. The immunological benefits are essential because the immune system is already working hard to keep a fragile balance between inflammation and suppression because of the burns. Probiotics help the body heal from systemic disorders and wounds by reducing inflammation and boosting the immune system (20).

Protecting microbiota, changing how the immune system works, and using probiotics to treat burn injuries are all parts of a complete plan to improve clinical outcomes. More and more evidence suggests that probiotic therapy may help burn victims heal faster and feel less pain. This is why it works well with other treatments for burns. Changes to the permeability of the intestines and the movement of bacteria A diverse and balanced gut microbiota is associated with health due to its regulation of immune responses to external antigens, its role in preventing pathogenic microbial invasion, and its influence on cytokine production (13).

People who have burns are more likely to have dysbiosis, which is an imbalance in the gut microbiota. Dysbiosis occurs when pathogenic bacteria, such as Enterobacteriaceae, outnumber commensal bacteria, like Lactobacillus and Bifidobacterium species (14). The microbiota of burn patients is further complicated by systemic inflammation, antibiotic administration, diminished gastrointestinal motility, and decreased blood flow to the gastrointestinal tract. These changes let endotoxins and pathogens get into the bloodstream from the gut (15).

Reduction of Nosocomial Infections

Health complications caused by infections contracted while in the hospital are a leading cause of death and disability among burn sufferers. The unique vulnerability of this patient group is the result of multiple interrelated variables. Among these are disruptions to the immune system, several invasive procedures, extended hospital stays, and significant loss of the skin's protective outer layer. When

combined, these factors create an ideal environment in which an illness might spread (21). The already high risk is exacerbated by the widespread and often necessary use of broad-spectrum antibiotics, which disrupt the gut microbiota and decrease colonization resistance, making patients more susceptible to opportunistic infections and MDROs (22).

A significant consequence of this disruption is gut dysbiosis, which increases intestinal permeability and decreases mucosal immunity. Translocation of infections and microbial toxins into the systemic circulation is made easier with a compromised gut barrier, which raises the risk of sepsis, multiorgan failure, and localized infections (23).

Using probiotics is an intriguing new way to reduce burn care infections. Probiotics help restore the microbial balance and maintain gut integrity while also supporting the immune system and reducing the vulnerability to bacterial colonization (24).

Their protective effects are mediated by multiple mechanisms:

As a result of competitive exclusion, pathogens are unable to attach to mucosal surfaces and cause an illness (25). Make antimicrobial compounds including bacteriocins, organic acids, and hydrogen peroxide, which directly inhibit harmful organisms (26).

Increased secretory IgA synthesis, improved antigen presentation, and balanced cytokine signaling are all ways in which the host immunological response can be regulated, leading to a more controlled and efficient immune defense (27). Limiting the loss of epithelial cells, improving intercellular connections, preventing bacterial translocation, and reducing systemic inflammation (28).

Probiotics may aid burn patients in reducing healthcare-associated infections (HAIs), according to mounting clinical evidence. One mechanism by which probiotics alleviate these infections and their potential systemic effects is by repopulating the gut with beneficial bacteria and thereby blocking the harmful effects of toxins. Probiotics also help in other ways, such as by influencing the urogenital flora and enhancing mucosal immune defenses. Finally, probiotics have the ability to decrease the occurrence of ventilator-associated pneumonia and other respiratory tract infections by regulating the gut-lung axis and improving systemic immunity. Supplementing with probiotics may slow the development and spread of MDROs by filling in beneficial bacterial roles in the digestive tract and reducing the need for broad-spectrum antibiotics (29). Along with reducing infection rates, this also helps.

Modulation of Sepsis Risk and Systemic Inflammation

On the other hand, severe sepsis continues to be the major cause of death, hospitalization, and

morbidity among people who have had burns. There are a number of mechanisms that contribute to the complicated pathophysiology of sepsis in this group of individuals. These mechanisms include severe tissue damage, prolonged systemic inflammation, immunological dysregulation, and microbial translocation from injured mucosal surfaces, particularly in the gastrointestinal tract (30).

When the immune system reacts to a severe burn, it becomes overactive and releases inflammatory cytokines such as TNF- α , IL-1 β , and IL-6. This causes the immune system to become overactive. The over activity of this cytokine storm, which was initially designed to reduce the risk of infection and injury to tissues, frequently results in endothelial dysfunction, capillary leakage, and involvement of organs (31).

In addition, probiotics contribute to the reduction of epithelial apoptosis, the maintenance of tight junction integrity, and the enhancement of mucus formation, all of which contribute to the strengthening of the gut barrier. These various elements are continually impacting one another in a reciprocal manner. The most common causes of sepsis in burn patients are endotoxemia and bacterial translocation; the use of these procedures reduces the risk of both of these conditions occurring (32).

It has been demonstrated in a number of studies that probiotics have positive benefits, which raises the idea that they may be able to alleviate some of the adverse consequences that are associated with sepsis. Patients who took probiotics had an improvement in their immunological profiles, a reduction in the number of bacteremia episodes that occurred, and a decrease in the levels of inflammatory markers in their bodies. These results suggest that probiotic supplements may be effective in burn care sepsis prevention programs (33) despite the fact that additional large-scale randomized controlled studies are required to be conducted. When all of these factors are brought together, the result is an environment that is optimized for the rapid spread of sickness (34). It is possible that the use of drugs that have a broad spectrum could lead to an increase in the prevalence of opportunistic infections and multidrug-resistant organisms (MDROs), both of which are previously common (35). This is due to the fact that they have the ability to change the gut flora and decrease colonization resistance.

This disruption has a number of serious effects, one of which is a dysbiosis in the gastrointestinal system. This dysbiosis lowers the mucosal immunity and makes the intestines more permeable. There are a number of consequences that can occur when microorganisms are able to get through the gastrointestinal barrier and into the bloodstream. These complications include sepsis, organ failure, and localized infections (36). A promising new

approach in the treatment of burns is the utilization of probiotics for the purpose of lowering the incidence of infections. There are many benefits associated with probiotics, two of which are the maintenance of the natural bacteria balance in the gut and the facilitation of the immune system (37). As one of the many preventive mechanisms that it possesses, competitive exclusion (38), they reduce the likelihood that germs would cling to mucosal surfaces and cause sickness.

The elimination of harmful bacteria can be accomplished through the production of antimicrobial compounds, such as bacteriocins, organic acids, and hydrogen peroxide (39).

It is possible to modulate the immunological response of the host in order to increase the generation of secretory IgA, the presentation of antigens, and the balance of cytokine signaling (40). By doing so, we will be able to cultivate an immune defense that is more under control and efficient.

Reducing systemic inflammation, decreasing the loss of epithelial cells and intercellular connections, and limiting the transmission of germs are the mechanisms by which these objectives can be accomplished (41).

Additionally, probiotics have a wide variety of other positive effects on the body. In conclusion, probiotics have the potential to reduce the requirement for hospitalization due to respiratory infections such as pneumonia by enhancing the immune system as a whole and altering the relationship between the gut and the lungs. In order to reduce the development and spread of MDROs, one method that can be utilized is to take probiotic supplements (42). Due to the fact that they are able to perform a useful function as bacteria in the digestive system, they reduce the need for antibiotics, which are capable of warding off a wide range of illnesses. It is possible to lessen the likelihood of infection, which is an exciting additional benefit. Severe sepsis is a leading cause of death, hospitalization, and overall morbidity and mortality in burn victims. This is due to the fact that it causes a high rate of fatalities. In this particular population, the complicated pathophysiology that leads to the development of sepsis is comprised of severe tissue destruction, prolonged systemic inflammation, immunological dysregulation, and microbial translocation from wounded mucosal surfaces (especially the gastrointestinal tract) (43). There is a correlation between each of these factors and the onset of sepsis.

In the aftermath of a severe burn, the immune system experiences a spike of inflammatory cytokines, which include TNF- α , IL-1 β , and IL-6. This surge causes the immune system to become hyperactive. It is possible for this cytokine storm to cause endothelial dysfunction, capillary leakage, and organ involvement when it becomes excessive.

This is despite the fact that its primary objective is to reduce tissue damage and infection (44).

Intestinal barrier enhancement is further supported by probiotics through the reduction of epithelial apoptosis, the rise in mucus production, and the maintenance of the integrity of the tight junction area. In burn patients, bacterial translocation and endotoxemia are two of the most common causes of sepsis (45). These approaches have the potential to ameliorate both of these conditions.

Patients whose therapy included probiotics demonstrated improved immunological profiles, lower inflammatory markers, and fewer incidences of bacteremia, according to the findings of several investigations. A conclusion that can be drawn from these data is that probiotics have the potential to lessen the severity of the difficulties that are linked with sepsis. In spite of the fact that additional large-scale randomized controlled studies are required, these findings suggest that the incorporation of probiotic supplementation into burn care sepsis prevention strategies may prove to be advantageous (46).

For those who have suffered from burns, healthcare-associated infections remain the leading cause of death and physical disability. Specifically, this is due to the fact that infections are the most prevalent of all medical conditions. This particular patient population is extremely vulnerable due to a complex web of interconnected factors that contribute to the state of affairs. Alterations to the immune system, several invasive surgical operations, prolonged hospital stays, and significant epidermal degradation are some examples of the complications that can arise. In the event that all of these elements come together, there is an increased probability of disease transmission (47), which is one of the fundamental reasons. The widespread use of broad-spectrum antibiotics, despite the fact that they are necessary, has a deleterious impact on the microbiota in the gut, which in turn diminishes colonization resistance and makes opportunistic infections and MDROs worse (40).

The dysbiosis that occurs in the gut is the most obvious result of this imbalance. This dysbiosis leads to a reduction in mucosal immunity and an increase in intestinal permeability. In patients who have damage to their gut barrier, the risk of developing sepsis, failure of several organs, and localized infections is significantly increased. It is possible for certain bacteria and pathogens to pass through the intestinal barrier and enter the bloodstream, which is the reason for this phenomenon (41).

One novel and intriguing strategy to the treatment of burns could be to make use of probiotics in order to lower the incidence of infections. For example, taking probiotics can help improve the immune

system, maintain a healthy balance of bacteria in the gut, and keep the gut healthy (42). This is just one of the many benefits of taking probiotics. It has been suggested that competitive exclusion is one of the mechanisms that mediates the protective effects of pathogens (43). By virtue of this process, viruses are unable to attach themselves to mucosal surfaces and so prevent human infection. Bacteriocins are another example of an antibacterial agent, and hydrogen peroxide is yet another example (44). An organic acid is an example of an antibacterial agent. There is a possibility that you could manufacture these chemicals.

An immune defense that is more regulated and effective can be achieved by managing the immunological response of the host, which involves increasing the production of secretory IgA, enhancing the presentation of antigens, and maintaining a balanced cytokine signaling system (45). Maintaining control over the immunological response of the host is one approach that can be taken to achieve this goal. The reduction of systemic inflammation, the reduction of epithelial cell loss, the strengthening of connections between cells, and the reduction of bacterial translocation are some of the things that are involved in this process (46).

According to the findings of recent clinical trials, probiotics may have the potential to lower the number of healthcare-associated infections (HAIs) that occur in burn patients. Additionally, the possible systemic impacts of these disorders can be minimized with the assistance of probiotics, which allow for more effective management of these conditions. In order to achieve this goal, good bacteria are reintroduced into the digestive system, which in turn reduces the severity of infections. In addition to modifying the bacteria that are present in the urogenital tract and boosting the immunological defenses of the mucosal barrier, probiotics have a number of other beneficial effects. The use of probiotics has been shown to reduce the incidence of respiratory tract infections, particularly pneumonia associated with the use of ventilators. It is necessary to make adjustments to the gut-lung axis and to strengthen the immune system in order to achieve this goal. According to the findings of some research (48), taking probiotic supplements may result in a reduction in the quantity of MDROs that are created and transported throughout the body (49, 50). To achieve this goal, beneficial bacteria that live in the gut have the ability to take over and cover the bases in the event that antibiotics are ineffective. In addition to being helpful, it also helps to reduce the number of infections that occur (51, 52).

Enhancement of Wound Healing and Tissue Regeneration

The process of wound healing is a multi-step

procedure that includes hemostasis, inflammation, proliferation, and tissue remodeling. Typically, burn injuries are accompanied by significant tissue damage, a higher risk of infection, and immunological dysregulation, all of which might make this process more challenging (53). The inflammatory phase, which is a very carefully balanced portion of the process, might result in hypertrophic scarring that is not under control, wounds that do not heal, and a delay in the healing process. It has been proven that probiotics can boost wound healing responses through a variety of mechanisms, including metabolic remodeling, inflammatory management, collagen synthesis increase, matrix remodeling regulation, and epithelium regeneration promotion (54). Probiotics have been shown to have these effects.

Modulation of Inflammatory Response in Wound Healing

The removal of dead tissue, activation of immune cells, and beginning of the healing process after a burn all require inflammation throughout the healing phase. The opposite is true for keratinocyte function, surrounding sick tissue, and progression to the proliferative phase in an extremely severe or chronic inflammatory state. Probiotic bacteria may help keep the immune system from stepping in at the wound site by reducing the inflammatory response (55).

Evidence from multiple studies suggests that specific probiotic bacterial strains, such as *Lactobacillus rhamnosus* GG and *Bifidobacterium breve*, can reduce levels of inflammatory mediators like TNF- α and IL-1 β while increasing levels of cytokines that can control inflammation, like IL-10 and TGF β . Tissue repair and regeneration are aided by these immunomodulatory actions because they decrease inflammation (56). In addition, key growth factors such as transforming growth factor-beta (TGF- β) and vascular endothelial growth factor (VEFG) can be enhanced by using probiotics. In order to facilitate angiogenesis, fibroblast activation, collagen deposition, and epithelial cell proliferation, VEGF ensures that the nutritional and oxygen supply reaches the repaired tissue. When compared, TGF- β improves these procedures. These actions, when combined, shorten the duration of the inflammatory phase and speed up the healing process (57).

Collagen Synthesis and Extracellular Matrix Remodeling

Collagen formation and organization are in charge of rebuilding the structure and tensile strength of injured skin. To repair the extracellular matrix (ECM), stimulated fibroblasts predominantly create type I and type III collagens. Taking probiotics improves wound healing and tensile strength by increasing fibroblast activity and collagen formation. Because of this, probiotics

may exacerbate preexisting inflammatory diseases. Matrix metalloproteinases (MMPs) serve an equally significant role in promoting healing. Zinc-dependent proteases govern extracellular matrix remodeling. Fibrosis and ECM degradation have been linked to conflicts over matrix metalloproteinase (MMP) activity. It appears that probiotics affect matrix metalloproteinases (MMPs) and the proteins that inhibit them (TIMPs). Perhaps this will help manage the synthesis and breakdown of the extracellular matrix. This coordinated remodeling is critical for promoting normal tissue regeneration and preventing chronic wounds (59).

Epithelial Regeneration and Maintenance of Skin Integrity

An essential step in wound healing, re-epithelialization involves the migration and proliferation of keratinocytes, which restore the skin's protective barrier. A major hurdle to epithelial cell regeneration may be burn injuries, which damage the basal layer and cause long-term inflammation. The wound microenvironment and keratinocytes are two places where probiotics can affect the function of epithelial cells (60). Probiotics, when applied topically or taken orally, has been shown to hasten epithelial regeneration, decrease wound size, and shorten healing time in animal burn models. By increasing levels of epidermal growth factor (EGF) and causing cytoskeletal reorganization, some probiotic strains promote cell migration and proliferation throughout the wound bed. This is accomplished by elevating EGF levels. By enhancing local immunological monitoring and microbial defense, probiotics may aid in the avoidance of recurrent infections (61).

The long-term effects of probiotics on health and beauty are unclear. Reduced pathogenic inflammation, increased normal tissue regeneration, and decreased hypertrophic scarring are the means by which this is achieved. Burn victims can benefit greatly from this technique because reducing scarring is a crucial aspect of both their physical and mental recovery (62).

DISCUSSION

Multiple sclerosis remains a complex disease in which the interplay of inflammation, demyelination, and neurodegeneration progressively undermines neurological function. While current immunomodulatory therapies effectively reduce relapse rates and new lesion formation, they fail to halt the insidious accumulation of disability in progressive disease (63). This therapeutic gap underscores the urgent need to shift the focus from inflammation control alone toward strategies that actively promote remyelination and neuroprotection (64).

Challenges of Endogenous Repair

Despite the presence of oligodendrocyte precursor cells (OPCs) within demyelinated lesions, their capacity to develop into mature myelin products-called oligodendrocytes-is significantly impaired in chronic MS. Inflammatory mediators, oxidative stress, and oxidation of the extracellular matrix form a microenvironment actively inhibitory to OPC differentiation⁶⁵. Astrocytic scar formation and ongoing activation of microglia further enhances these inhibitory signals. Collectively, these trusts are taken to explain why remyelination is often robust in early disease but become inefficient or absent in progressive stages. Importantly, this progressive failure of repair is not a by-product of chronic inflammation, but a key pathomechanism in long standing neurodegeneration (66).

Limitations of Conventional Therapies

Approved disease-modifying therapies (DMTs) such as interferon-beta, glatiramer acetate and high-efficacy monoclonal antibodies generally target the immune system (67). Although they are highly effective in relapsing/tremolating MS, the failure to restore myelin acquisition leaves negative patients lacking with irreversible latent cheating of axonal damage. Moreover, the substantial patient-to-patient variability in response underscores the biological heterogeneity of MS, and an emphasis on precision strategies that go beyond immune modulation⁶⁸.

Emerging Remyelination Approaches

A number of novel strategies are being studied to directly stimulate repair. Stem cell-based therapies such as mesenchymal, neural and induced pluripotent stem-cell based approaches initially hold promise to help with replenishment of oligodendrocyte pool, and trophic support. Early-phase clinical studies provide a sense of feasibility and potential improvements in function, but there are concerns related to the engraftment of the cells, the immunogenicity, the long-term integration and the potential for it to turn cancerous (69).

Pharmacological and biological agents provide the alternative way. Growth factors like IGF-1 and FGF-2 or small molecules like clemastine fumarate have shown promise in improving the differentiation of OPCs, and remyelination (70). However, it had been difficult to translate such findings into consistent clinical benefit, such as seen with the use of anti-LINGO-1 therapy (opicinumab), which despite a strong preclinical rational had poor efficacy. These experiences point toward the complexity of remyelination biology, and the difficulty with single target interventions^m (71).

Gene therapy, nanotechnology are turning out to be the particularly attractive ways. Gene-editing tools

and viral vectors allow for the targeted grading of signaling pathways that dictate the fate of OPCs, and nanocarriers provide novel solutions to surmount the restrictive blood-brain barrier and treat therapeutics to demyelinated locations. Although these modalities are still in an experimental phase, they reflect a paradigm shift into more precision, localized CNS repair (72).

Challenges and Future Directions

In spite of the fact that probiotics have shown some promising outcomes when used as an adjuvant therapy within burn care, there are still a number of substantial obstacles to overcome before the widespread implementation process using probiotics in clinical practice can be concerned or carried out. One of the biggest problems is identifying the probiotic strains that are the most effective (73). Not all probiotics have the same impact in terms of immunological modulation, gut barrier integrity or wound healing. This is because there is a wide variety of probiotic species and strains that each have their own unique set of biological activities. Due to the fact that the available information is inadequate and often inconsistent, it is of the utmost importance to decide what strains or mixtures of strains are most beneficial to burn patients (74).

The issue of how to find the optimum dosages and means of delivery is another major obstacle to clear up. There is no agreement amongst experts on the best concentration, dosing frequency, and treatment time duration for probiotics in order to induce obvious therapeutic effects. This is because there is not a general agreement concerning these factors. The clinical decision-making process is made even more difficult because these criteria range from trial to trial, giving trials inconsistent results. In addition, the effect of probiotic administration on colonization and efficacy of these treatments is unknown in burn patients (75). This is regardless of whether probiotics are best supplied topically or orally-or even the ideal combination of the two.

A major complication is that many drugs, most notably antibiotics, have a negative interaction with probiotics. Burn patients must take antibiotics to ward off infections, but these drugs may deplete the efficacy and shelf life of probiotics without meaning to. It's important to consider whether probiotics will have antagonistic or synergistic effects, and when to deliver the probiotics, if we want the highest possible therapeutic results from antibiotic treatment (76).

CONCLUSION

The use of probiotic in burns treatment is an interesting new field of research with a great impact in enhancing results for burn victims. Probiotics can potentially accelerate the healing of burns through

restoration of a balanced microbiome, reduction in inflammatory and immunological processes and facilitate wound healing. While there may be promising advances we must act quickly to fund well-known designed studies if we are to find successful medications and their working. Integrating probiotics into current burn treatment protocols on a daily basis have the potential to be the norm in the future.

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