



Original Research

Low Level Laser Therapy (LLLT) Mechanism of Action, Application and Laser Light Therapy Devices in Physical Therapy

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Abstract:

"Light Amplification by Stimulated Emission of Radiation" is what the acronym "laser" stands for. Various light sources, such as light-emitting diodes, have entered the laser arena. A wide variety of red and near-infrared light waves are employed. The target tissues are affected differently by each wavelength. Research on low-level laser treatment (LLLT) is booming as a potential solution to the problems caused by high-dose lasers. A variety of cells in the body are directly bio-stimulated by low-level laser therapy. It has been found that low-level laser therapy (LLLT) can speed up the healing process for wounds and also stimulate bone cells, which means that bones can recover more quickly.

Stimulated emission of radiation is the process that produces laser light. Laser light has numerous distinguishing features, including great intensity, homogeneity, and the fact that it travels in a straight line, all of which contribute to its targeted interactions with biological tissues. Presenting a wide range of laser applications in pharmacy and medicine, this study also aims to describe the fundamentals of lasers and how they interact with tissues. The biostimulation effects of low-level laser therapy include an elevated core body temperature, enhanced blood circulation, and accelerated metabolic rate. Treatment with high-powered lasers causes photothermal effects. This tissue undergoes fotoablation and fotocoagulation when exposed to that particular wavelength of laser light. Lasers can be either continuously operating or releasing light pulses at a specific frequency. The laser's active centre can be made of a variety of materials, including solids, liquids, semiconductors, or gases. The medical and pharmaceutical fields are well-known for their extensive use of lasers. Many medical fields make use of lasers, including dermatology, ophthalmology, stomatology, laryngology, and neurology, due to their ability to reduce bleeding, make precise cuts, ensure improved visibility during operations, lessen pain, and speed up the healing process after injuries. The impact of laser biostimulation on the efficacy of pharmaceutical treatments.

A relatively new method for wound healing is low level laser therapy (LLLT). Current approaches for treating wounds with laser radiation and clinical concerns for various wound types are reviewed in this paper. We also quickly go over the hypothesised ways in which LLLT aids in the healing of wounds. Additional controlled trials are required to clarify the many stages of the healing process and objectively determine the influential parameters of LLLT, while numerous studies have improved our understanding of the laser healing process.

The effects of LLLT are still up for debate, despite numerous reports of positive results from in vitro studies, animal models, and randomised controlled human trials. Contrarily, more studies are required to determine whether periodontal therapy is effective.

Introduction:

The "Light Amplification by Stimulated Emission of Radiation" (or "Laser") has been a mainstay of modern dentistry for almost three decades. Because of its three unique characteristics—that it is monochromatic, coherent, and collimated—laser light is very powerful. That first "Microwave amplification by stimulated emission of radiation (MASER)" laser was created in 1960 by Theodore H. Maiman. The way in which a laser interacts with tissue determines its classification as either a hard tissue laser or a soft tissue laser, rather than the exposed tissue type [1]. As a kind of physical therapy, low-level laser therapy (LLLT) uses light-emitting diodes or low-level lasers to change cellular processes. Laser acupuncture, biostimulation, therapeutic, low-power, cold, and soft tissue lasers are some of the many names given to low-level laser therapy. Lasers can be anywhere from 1 to 500 mW on average, with wavelengths spanning 600 to 1000 nm (red to near infrared). To stimulate different tissues and boost cell function, low-power lasers are used instead of high-power lasers, which ablate tissue. Analgesic effects are among the biological therapeutic benefits of low-level laser therapy, which is a painless and noninvasive procedure that employs photonic radiation [2-4]. Pain associated with myofascial regions, healing from fractures, tendinous or ligamentous injuries, postoperative incision care, tissue necrosis, nerve damage, osteoarthritis, and other chronic pain syndromes. Paraesthesia, periodontitis, dentinal hypersensitivity, temporomandibular joint disorders (TMD), pain during orthodontic tooth movement, oral lichen planus, xerostomia, mucositis, and recurrent aphthous stomatitis (RAS) are some of the dental conditions treated with LLLT.

Why Low-Level Laser Therapy (LLLT)

Works:

The exact mechanism of action of LLLT is not well understood, but it has been demonstrated that it has the potential to alleviate inflammation-related pain by reducing levels of various inflammatory markers in a dose-dependent

fashion, including prostaglandin E₂ (PGE₂), interleukin-1 beta (IL-1 beta), tumour necrosis factor-alpha (TNF-alpha), cellular influx of neutrophils and granulocytes, oxidative stress, congestion, and haemorrhage.¹ Doses of LLLT can be anything from 0.33 to 19.0 J/cm². Cells are stimulated by low-level laser therapy at low dosages and suppressed at large dosages [5, 6]. A second theory is that it works by influencing redox signalling, which in turn affects intercellular homeostasis and cell proliferation, by encouraging the mitochondria to produce more ATP, which raises the levels of reactive oxygen species (ROS).² Reducing edoema through altering capillary hydrostatic pressure, low-level laser treatment also influences microcirculation [7]. New endothelium and blood vessels are produced by the optimal dosage of LLLT, which aids in the creation of granulation tissue and speeds up the healing process. Pain and spasms in the affected muscles are alleviated through the relaxing of smooth muscles in various systems brought about by low-level laser therapy.

Procedures Angiogenesis:

Angiogenesis and the maturation of vascular endothelial cells are both aided by infrared light.⁵ When thinking about tissue healing and using a laser on highly vascularized tissues, this quality is crucial. Highly vascular tissues, such as neoplasms, should not be treated with a laser. While Dourado et al. found angiogenesis to be enhanced at both 633 and 904 nm, they found that 633 nm had a stronger response at lower doses and that higher doses of 633 nm were less effective than 904 nm. Similarly, Cury et al.⁶ showed that both 660 and 780 nm were beneficial, however, the shorter wavelength was only helpful at larger dosages, while the longer wavelength was effective at both low and high levels [8].

Changes in Vasodilation:

By relaxing smooth muscles, which leads to vasodilation, low-level laser therapy has the potential to enhance local circulation. This may occur as a result of perivascular tissue-specific NO₂ induction. Researchers Carrera et al.⁹ found that acute surgical wounds treated with laser

therapy exhibited greater vasodilation. No change in local circulation was found in healthy tissues in the study by Heu et al. Lasers have the potential to enhance the erythrocyte molecule's deformability, according to an earlier study by Mi et al. This could lead to faster erythrocyte movement via peripheral capillary beds and more haemoglobin molecules available within red blood cells.

Efficacy in Healing Wounds:

Many different types of cells in the body are stimulated by LLLT. Increases in metabolism, migration, and proliferation, as well as increases in protein synthesis and secretion, are the main cellular responses seen in vitro following LLLT. Researchers have found that low-level laser therapy can widen blood vessels and boost blood flow to certain areas. The increased flow of oxygen and immune cells into the tissue is facilitated by this vasodilation. Both of these effects help the body repair more quickly [8, 9]. Varying cell types may have varying wavelength responses, although it seems that the majority of cells are sensitive to light between 630 and 980 nm. Osteoblast cultures respond better to 790 to 830 nm range laser light than 660 to 690 nm range light at equal doses; yet, 632 nm light at 0.43 J/cm² induces an increase in osteoblast numbers and activity in cell cultures. Similarly, light at 904 nm did not have any discernible impact. Phototherapy in the 630–690 nm range, according to published studies, increases adhesion and endothelial cell proliferation. Cell cultures seem to be most responsive to moderate levels of infrared radiation, according to a small number of in vitro investigations; nevertheless, the optimal dose may vary across cell types: In fibroblasts, it is approximately 15 J/cm²; in keratinocytes, it is 3 J/cm² (at 780 nm). Increasing the dosage basically had the opposite impact in every instance [10, 11]. A small number of researchers have postulated that multiple laser treatments spaced 24 hours apart might have an additive impact.

It was recently shown by Akgul et al. that delaying the start of LLLT after the acute inflammatory phase yielded superior outcomes. A

study conducted by Farouk et al. examined the effects of several laser wavelengths on the healing process of oval full thickness wounds in Sprague-Dawley rats. The results showed that the wounds closed 7.7 to 29% faster in healing days. The greatest acceleration in healing days (29%), measured in nm, was achieved using a 632.8 nm HeNe laser. The results of this study demonstrated that photons in wound healing rely on wavelength, treatment schedule, and dose. There is no correlation between laser skin transmission and the accelerated healing of wounds [12-15] because fibroblast absorption and wound healing are both at their peak at 632.8 nm. For optimal wound healing acceleration, an incident power density of 10.53 mW/cm² from a 632.8 nm HeNe laser was shown to be non-dose rate dependent.

LLLT and Wound Care:

As a kind of laser medicine that uses low level (low power) lasers or light emitting diodes to change cellular activities, LLLT is pushed for its therapeutic effects in treating wounded tissues and suppressing pain [16]. Acute discomfort, surgical incision scars, and the stimulation, fortification, and commissioning of the cellular cycle to produce productive and replacement cells are all areas where LLLT has shown to be quite beneficial. LLLT uses low-dose lasers to influence cellular immunity, enzymatic chain reactions, cell proliferation, tissue secretions, etc. with minimal systemic adverse effects and maximum therapeutic impact.

Limits of the LLLT Physical Model:

The dispersion of electromagnetic radiation with specific properties—monochromaticity, coherence, and low divergence—is the most essential physical attribute of a laser that makes it suitable for medical therapy. Monochromaticity refers to the laser's intensity, which is connected to its spectrum distribution; however, this is not an essential feature for LLLT applications. Introducing energy into a medium in order to excite it is a good way to characterise a laser's operational scheme [17]. The absorption process is the most important part of the laser beam's interaction with tissue. A spectrally narrow laser is

not absolutely necessary due to the wide width of the absorption bands.

Interaction between Biological Tissues and Lasers:

Laser interaction with biological tissue mostly results in thermal and non-thermal effects, similar to any other electromagnetic treatment. Non-thermal energy applications are essentially what LLLT is. The term "non-thermal" is used to describe situations where there is no net increase in temperature on a macroscopic scale, even if the body will generate some heat as a result of any energy that is delivered or absorbed. One popular name for LLLT is photobioactivation, which means to stimulate different biological processes by means of light energy without causing substantial temperature changes. Photobiostimulation and photobiomodulation are two more synonyms [18]. A photon, or laser beam, changes an atom's energy level from e_2 to e_3 , which results in a shift in physicochemical cellular function and sets off a mimetic cascade mechanism. Along the same path as the stimulated photon will go a second, in-phase photon. Laser light creation is based on this phenomenon, which is called stimulated emission. Earlier it was noted that the majority of biological tissues preferentially disperse photons in a forward orientation.

There are a variety of medicinal uses for laser light because of its distinctive properties. A few key characteristics are polarisation, coherence, and monochromaticity. Among these factors, monochromaticity has the greatest impact on the therapeutic outcomes. Researchers have postulated three primary reactions—photochemical, photothermal, and photoplasma—as the result of laser interactions with tissues [19]. The photochemical reaction involves the temporary inactivation of cell function as a result of the hazardous chemical procedures caused by extremely low-power irradiation. Tissue chromophores absorb light in this type of interaction, and when local temperature rises, conduction to cooler regions begins. Denaturation, necrosis, vaporisation, and spallation are all

possible outcomes of an extremely high temperature. [20] Though they do not absorb it directly, biomolecules like DNA and RNA can have their activities altered by exposure to low-intensity visible light. It is likely that the energy is mainly absorbed by the cell membrane, which subsequently causes effects to occur within the cell through a cascade or second messenger reaction. According to reports, the condition of the cells and tissues before irradiation plays a role in determining the strength of this photoresponse. A simple explanation could be that 'starving cells are more photosensitive than well fed ones' [21]. Therefore, it is believed that photosignal transduction causes the tissues to undergo changes in their metabolic processes in response to laser light irradiation. This suggestion is supported by the often-cited Arndt-Schultz Law.

What Makes LLLT Superior to Alternative Methods:

A complex and ever-changing process, wound healing is the body's normal reaction to damage to living tissues. Performing a thorough evaluation of the patient after therapy is an important first step in providing effective wound care [22–25]. This clinical operation in medication administration strategies is typically given higher weight by clinicians. There are systemic and localised effects of drugs used to treat wounds. Specific examination is necessary for systemic impacts and medication side effects. Applying LLLT gives us the chance to target particular regions, which means we can increase the likelihood of eliciting systemic effects, particularly on important organs. Wound healing mostly involves the application of electrical and magnetic stimulations [26, 27]. Although it has the potential to enhance flap and graft survival, speed up postoperative recovery, and reduce necrosis, electrical stimulation is underused as an adjuvant treatment in plastic surgery. Reducing infection and improving cellular immunity are two more potential benefits. Electrical stimulation has the added benefit of increasing tissue perfusion, which speeds up the healing process after a wound [28].

Rejuvenation Stimulants Using Peptides:

Proteins called short chain peptides are formed when collagen fibres break down. Matrix metalloproteins (MMPs), such as collagenase, have peptide feedback inhibitors. It is possible that fibroblasts can be stimulated to generate collagen by small peptides (3-5 chain amino acids). Cosmetics have already begun to incorporate some of these chemicals. The chemical known as Matrixyl®, for example, consists of a carrier molecule and five amino acids. There is evidence that this molecule, which is a portion of type 1 procollagen, can stimulate fibroblasts to produce more collagen [29]. Fibroblasts are instructed to increase collagen production by this short chain peptide, which is a component of a positive feedback loop. We can expect to see more and more signal peptides in cosmeceutical solutions as our knowledge of them grows. The ability of senescent fibroblasts to make type 1 collagen is known to be decreased. In the phase of healing that follows an injury or heat stimulation, however, these fibroblasts can be activated to enhance collagen formation. Several chemicals, including a large number of peptides, signal the fibroblasts to increase their activity during this period. As an example, the amount of collagen mRNA increases after ablative laser resurfacing. One way to achieve the rejuvenating benefits of resurfacing without undergoing the process is to develop a cosmeceutical that uses the peptides and cytokines released after laser treatment. More specifically, we know which peptides cause fibroblasts to become more active. But getting bigger molecules across the epidermal barrier isn't easy. There have been recent advancements in the capability to transport big molecules over the epithelial layer. As an example, it has only lately become possible to administer botulinum toxins topically [30]. With this novel delivery capabilities, wound healing peptides and cytokines can be even more successful as cosmetic components. The activity of enzymes that break down collagen increases with age in the skin. Inhibiting collagenase using cosmeceuticals or oral drugs can tip the scales in favour of younger, more abundant collagen. Collagenase (matrix

metalloproteinase 1, MMP-1) has its enzymatic activity reduced by the use of several inhibitors. Matrix metalloproteinase inhibitors and low-dose antibiotics like sub-antimicrobial doxycycline are two examples. These compounds are currently administered orally, however they have the potential to be used as cosmeceutical components due to the signal peptides they induce. Collagen matrix fragmentation is another telltale sign of skin that is getting older. Collagenase and other matrix metalloproteinases are to blame for this [31]. As a result of dermal matrix collapse, fibroblasts are no longer supported, and they regress, producing enzymes that breakdown collagen instead of the substantial amounts of collagen they once did. Laser resurfacing and other rejuvenating operations, together with renovating drugs like tretinoin, can promote collagen formation, which in turn can anchor fibroblasts and restore a younger dermal structure, according to the authors of this study. Important players in this cascade include cytokines and peptide compounds, which have the potential to be highly effective cosmetics.

Promoting Youthful Cellular Machinery via Cytokines and Signal Peptides:

After collagen and other structural fibres break down, short chain peptides—which are chains of amino acids—are generated. It is possible that these peptides inhibit matrix metalloproteinases (MMPs) by feedback effect. Several commercial preparations have made use of short chain amino acids, which may encourage fibroblasts to manufacture collagen. The chemical known as Matrixyl®, for example, consists of a carrier molecule and five amino acids. There is evidence that this molecule, which is a piece of type 1 procollagen, can stimulate fibroblasts to produce more collagen [31]. The pieces reflect degraded collagen that needs replacement at the cellular level. Therefore, this short chain peptide may serve as a positive feedback loop, telling the fibroblasts to generate more collagen. There will be an increase in the use of these peptide compounds in cosmeceuticals as the signals sent to fibroblasts are intercepted and understood. Peptides have the potential to transport many

different compounds. An example of a material that peptides bind to is copper. There are now cosmetics on the market that contain copper-peptide complexes; one such compound, GHK, which stands for glycyl-histidyl-lysine, offers numerous desirable cosmetic effects. The cells that are in charge of healing and renewal require metals (like magnesium) that are not copper. The development of peptide complexes with additional metals and catalysts is anticipated to yield compounds with enhanced cosmeceutical properties.

Physical therapy laser light therapy devices for:

- **Generalised Chronic Pain:** Disabilities due to chronic pain occur more frequently than any other condition. About 76.2 million people experience acute discomfort that lasts more than 24 hours, according to the National Centre for Health Statistics. Inflammation, stiffness, tension, muscular spasms, and other forms of chronic pain are all part of the same category. On multiple levels, LLLT alleviates chronic pain and its associated symptoms. When you use LLLT, you can alleviate a lot of symptoms, including pain, inflammation, spasms, pains, stiffness, and tension in your muscles. Enhanced blood and lymph circulation, more mobility, and suppleness of tissues (such as scar tissue) are additional advantages. Depending on the region's size and the dosage offered by the cold laser unit, the laser is held directly over the damaged area for 30 seconds to several minutes. Theoretically, this light energy triggers a cascade of biological reactions that normalise wounded or damaged tissue, decrease inflammation, edoema, and healing time by enhancing intracellular metabolism.

- **Pelvic Dysfunction:** When the pelvic floor muscles are tight or weak, or if there is an impairment of the sacroiliac joint, low back, coccyx, or hip joint, a variety of difficulties can arise. Pain in the pelvis could be due to heightened or diminished sensitivity and/or irritation of the tissues around the pelvic organs. A cold laser is a type of low-intensity laser that may aid in the

reduction of inflammation, discomfort, and the speed of wound healing. In addition to relaxing muscular spasms and increasing local blood flow where they are constricted or pinched, LLLT can alleviate mild aches and pains in the muscles, joints, and tendons.

One out of five Americans are afflicted with arthritis at this time. Pain relievers and anti-inflammatory medications are the mainstays of arthritis treatment, but they come with serious side effects including increased risk of cardiovascular disease, stroke, renal disease, and stomach bleeding. Taking these medications for an extended period of time increases the chance of long-term negative effects, even if they are only meant for short-term usage. However, this is obviously not an option for anyone with arthritis [32]. Rheumatoid and osteoarthritis have both shown improvement after LLLT, because to the technique's ability to change cellular function. A recent study published in *The Journal of Rheumatology* found that LLLT significantly reduced pain, morning stiffness, and enhanced hand flexibility in patients with rheumatoid arthritis compared to a placebo. Research out of the United Kingdom's University of Dundee found that osteoarthritis sufferers reported much less pain after receiving laser therapy that stimulated the same pressure points as acupuncture. People used a scale from 1 to 10 to rate how much discomfort they were in. Results were reported in *The Journal of Physiotherapy* and demonstrated that treatment resulted in a 1.3 point decline in pain scores on average and a 2.4 point drop in some cases.

- **Achilles tendonitis:** This injury often occurs in athletes. Roughly 11% of runners experience this type of injury. When the discomfort is severe, Achilles tendinitis can make walking and running extremely painful, if not impossible. Achilles tendinitis is more common in recreational athletes in their middle years compared to younger age groups. For the same reasons that other tissues in the body becoming less pliable and more prone to damage with age, the Achilles tendons do the same. The most common causes of Achilles tendinitis include changes in running technique or

footwear, excessive pronation of the foot, and overuse injuries. Achilles tendinitis most commonly manifests as discomfort in the back of the heel. Conventional tendonitis treatments include resting the injured tendon and using ice to reduce inflammation; however, research indicates that LLLT can offer pain relief and speed healing. Lasers in Surgery and Medicine also reported that using ultrasound in conjunction with LLLT sped up the healing process and increased the tensile strength of the tendon.

Up to three percent of the population experiences lateral elbow tendinopathy, also known as tennis elbow, as a result of an overload injury that frequently follows mild damage to the extensor forearm muscles. Tennis elbow can cause chronic pain and symptoms for up to 20% of patients, which can last for more than 18 months to 2 years. Patients with a poor prognosis due to failed steroid injections or other treatment failures, long symptom duration, or severe baseline pain were included in a review of studies published in BMC Musculoskeletal Disorders. The review found that LLLT had an anti-inflammatory effect in 21 out of 24 controlled laboratory trials and a bio-stimulatory effect on collagen production in 31 out of 36 trials. Inducible at any wavelength between 630 and 1064 nm, with very small differences in therapeutic dose-ranges between wavelengths, these effects were shown to be dose-dependent, according to the research. This suggests that larger therapeutic doses of LLLT generate more collagen fibres and have an anti-inflammatory impact.

Persistent pain, numbness, and tingling are symptoms of Carpal Tunnel Syndrome (CTS), which originates from nerve issues in the wrist. Eventually, these CTS symptoms can grow so severe that they make it impossible for a person to work and may necessitate surgical intervention. In the United States, some 260,000 operations for carpal tunnel syndrome are carried out year. On the other hand, CTS can be reversed with prompt medical attention. Nerve insulation can wear away without treatment, which increases the risk of irreversible nerve injury and, ultimately, the necessity of surgery. Patients suffering from

carpal tunnel syndrome reported considerable improvements in grip strength, functionality, and pain levels after undergoing low-level laser therapy, according to a new study published in The National Centre for Biotechnology.

Pain in the tempromandibular joint (TMJ) is a common and serious issue. Jaw pain affects almost 10 million Americans. Jaw movement is guided by the temporomandibular joint (TMJ). Temporomandibular joint disorder or dysfunction refers to issues with the TMJ. Posture issues, prolonged jaw clenching, misaligned teeth, fracture, surgery, or "lockjaw" are among the many potential causes of TMD. When the discomfort from TMD spreads to other parts of the body, it can lead to a cascade of other issues. Symptoms of temporomandibular joint disorder (TMD) include jaw pain, exhaustion, trouble opening the mouth, and tinnitus. The low-level lasers used in LLLT have the ability to change cellular function, alleviate pain and inflammation, and enhance jaw joint flexibility when used to treat TMJ. Evidence from LLLT's anti-inflammatory, healing, and analgesic effects in TMJ and the masticatory muscle painful area was found in a meta-analysis of trials that included a placebo-controlled and double-blind design. It should be mentioned, nevertheless, that the amount of pain that LLLT can alleviate depends on the dosage.

• **Diabetic neuropathy:** Of all the complications that can arise from diabetes, this is the most common one. Sixty to seventy percent of diabetic people get diabetic neuropathy. A patient's standard of living can be significantly diminished by neuropathy. There is a 25–50 percent higher mortality rate and a 1.7-fold higher risk of amputation in diabetes individuals with neuropathy compared to diabetic patients without neuropathy. Modern treatment for diabetic neuropathy focuses only on alleviating symptoms, such as pain, by using a variety of analgesics. However, only around 40% to 60% of individuals report significant improvement in their symptoms after using these medications. Nevertheless, LLLT has demonstrated efficacy in treating diabetic neuropathy in studies. After four weeks of LLLT

treatment, patients reported a 26.4% reduction in pain, according to a research published in The Journal of Advanced Research. Theoretically, the analgesic benefits stem from a cascade of factors, including enhanced blood circulation, anti-inflammatory effects, elevated serotonin and endorphin levels, elevated cellular oxygen consumption, and enhanced mitochondrial ATP synthesis.

In The End:

Among the many noninvasive, appealing, and painless treatment options for modulating inflammation in dentistry, low-level laser therapy stands out. The field of biostimulation is constantly developing. The workings of low-level lasers are becoming clearer by the day. As an auxiliary treatment modality, low-level laser therapy has several applications in dentistry. The oral cavity's hard and soft tissues are both positively affected, and it has fewer antagonistic effects overall. It is evident that LLLT can promote the activity of many kinds of cells, and that multiple effects can happen simultaneously. Looking ahead, LLLT has a bright future. Finding out how the wavelength, treatment time, and application site affect the LLLT's efficacy is equally important. Efforts to standardise treatment regimens should centre on examining the precise dosage needed for therapeutic outcomes. Many important problems about LLLT in wound healing have not been resolved despite extensive research on many elements of this technique. Important areas that require additional research include the precise processes of laser-tissue interaction, critical parameters that determine therapeutic outcomes, and the effectiveness of LLLT on various chronic wound treatments. Many types of chronic wounds, including skin wounds, diabetic ulcers, necrotic wounds, and others, respond well to LLLT treatment. More randomised controlled trials together with assessments at the molecular and cellular levels are required to fill gaps in our understanding of the precise mechanisms of action. One of the most effective ways to rejuvenate the skin is with peptides and cytokines. You can find them in cosmeceuticals as growth factors and other mediators right now. Botulinum

toxin analogues, HSPs, and retinoid mediators are anticipated to be included in future generations. The more we learn about these compounds and develop methods to penetrate the epidermal barrier, the more control we will have over how our skin looks.

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