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Innovative Method for the Delivery of Drugs Using a Painless Laser Epidermal System

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Abstract

This study discusses current advances in the use of nonablative and ablative lasers to improve medication absorption. This article carefully covers the ideas and enhancing processes of lasers, emphasising the technique's potential for dramatically improving medication absorption through the skin. To improve medication penetration, several wavelengths and kinds of lasers are used. The ruby laser, the erbium:yttrium:gallium:garnet laser, the neodymium-doped yttrium:aluminum:garnet laser, and the CO_2 laser are among them. A revolutionary approach for increasing topical/transdermal medication delivery is fractional modality. This possible application of the laser provides a new therapeutic for topical or transdermal application with high effectiveness. Further research with a large number of people or patients is required to confirm and clarify the findings in animal studies. Although the laser fluence or output energy used to enhance medication absorption is far lower than that used to treat skin problems and rejuvenation, the safety of employing lasers remains a concern.

Keywords: *- Lasers, Transcellular, Ruby laser, Fractional laser, Photothermalwave.*

INTRODUCTION

Light Amplification by Stimulated Emission of Radiation (LASER) is an abbreviation for Light Amplification by Stimulated Emission of Radiation. [1] A laser is a device that causes atoms or

molecules to emit light at specific wavelengths and then amplifies that light to produce an extremely narrow beam of radiation. [12] It is used to treat skin conditions such as acne scars, rosacea, port wine stains, vitiligo, and hair removal [1]. Lasers help to improve medication penetration, which improves drug delivery through the skin. The fundamental method is controlled disruption and ablation of the stratum corneum, which serves as the primary barrier to drug transport. A photomechanical wave and a photothermal effect are also responsible for improved medication delivery. The benefits of this technique include higher bioavailability, shorter treatment times, and faster recovery. The notion of employing laser methods to treat the skin has gained popularity in recent years. [2] Mid-infrared lasers are used to improve skin permeability. Lasers are classified into two types: ablative and nonablative, based on their affinity for water [3].

Ablative Laser

This is a wounding laser that removes the thin outer layer of skin (epidermis) and warms the underlying skin (dermis), causing new collagen fibres to form. The treated region appears smoother and tighter as the epidermis recovers and regrows. The carbon dioxide (CO2) laser, the erbium laser, and combination systems are examples of ablative therapies [12].

Nonablative Laser

This is a non-wounding laser that stimulates collagen development, which helps to enhance skin tone and texture over time. This method may be used with various lasers and intense pulsed light (IPL) systems [13].

DRUG PERMEATION PATHWAY VIA THE SKIN

The stratum corneum, the skin's outermost layer, serves as the primary barrier to drug penetration. It is made up of lipids and proteins, with phospholipids, glycosphingolipids, cholesterol sulphate, and neutral lipids being the predominant lipids [6]. Permeation through the stratum corneum has been proposed via three routes: intercellular, transcellular, and transappendicular (Figure 1) [7].

Intercellular route: The medication diffuses mostly via the lipid-rich "mortar" surrounding the corneocytes of the epidermis. This lipid matrix can establish a continuous path through the epidermis (avoiding entering the cells), however this route has been reported to be less efficient since the interdigitating brick and mortar arrangement increases the distance 50-fold

compared to the straight route via the stratum corneum. [25]

The transcellular pathway is thought to be hydrophilic in nature. It is made up of aqueous regions surrounded by polar lipids that form the channel walls. Drug molecules passing through this channel diffuse between corneocyte clusters through flaws that form water-filled holes. This track is mostly provided by intracellular keratins.

Hair follicles and other appendages such as sebaceous glands play a significant part in dermal/transdermal transport in the transappendageal route. This is due to the fact that follicles are an effective pathway for transporting medications into deeper skin layers. Hair follicles are also an intriguing therapeutic target since they are complex and dynamic three-dimensional structures [8].

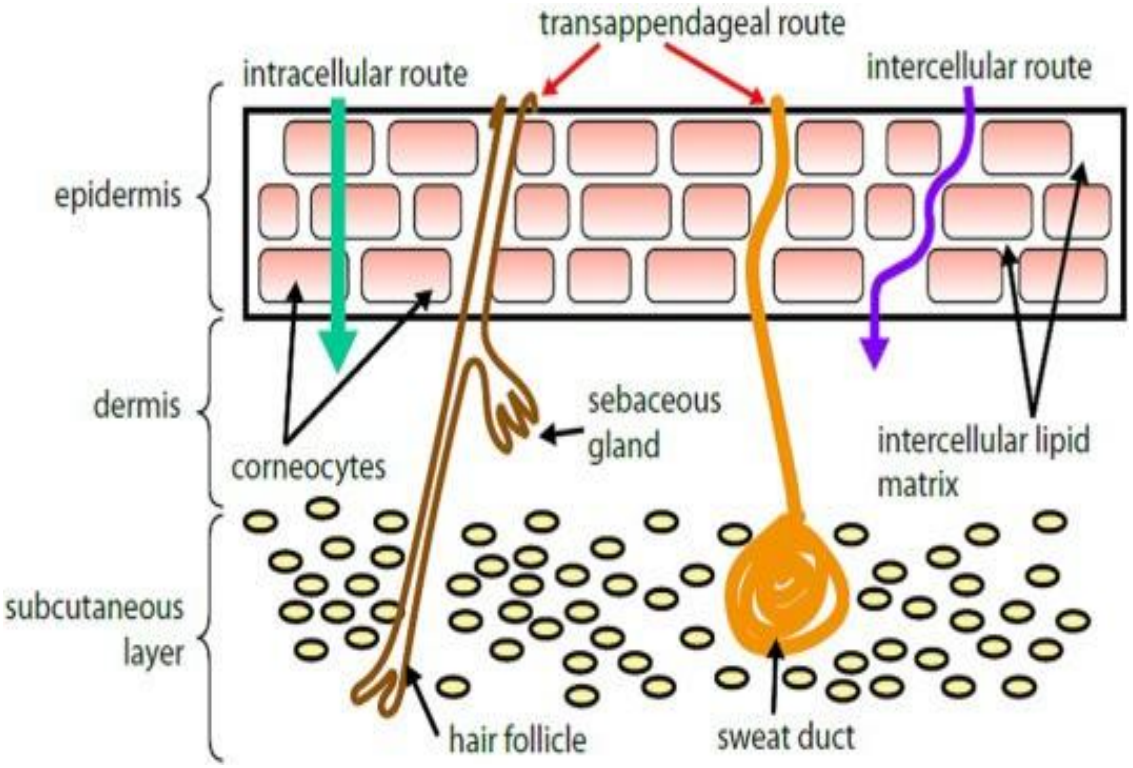

Fig.1. Different routes for drug permeation via the skin

MECHANISMS OF DRUG PERMEATION ENHANCED BY LASER

Enhanced percutaneous absorption of drugs occurs as a result of laser-skin interactions through three mechanisms: direct ablation, optical breakdown by photomechanical wave (PW), and a photothermal effect (Figure 2). In direct ablation, laser irradiation causes the skin target to decompose into small fragments that move away from the skin surface at supersonic speeds [11]. This ablation can significantly impair the barrier function of the SC, allowing drugs to pass through the skin more easily. PW is a unipolar, broad-band compression wave produced by lasers. PW causes lipid breakdown in the SC, allowing drug diffusion into deeper layers. PW also affects the cell plasma membrane, opening up transcellular pathways for drug transport across the skin [11]. Some lasers, such as the CO2 laser, have a considerable photothermal impact. Water readily absorbs the CO2 laser, which has a wavelength of 10,600 nm. If a large amount of light energy is delivered in a short period of time, it can be converted into heat, which quickly heats the skin tissue and causes vaporisation [11]. The heat effect impairs the skin barrier function, allowing medicines to penetrate the skin more easily.

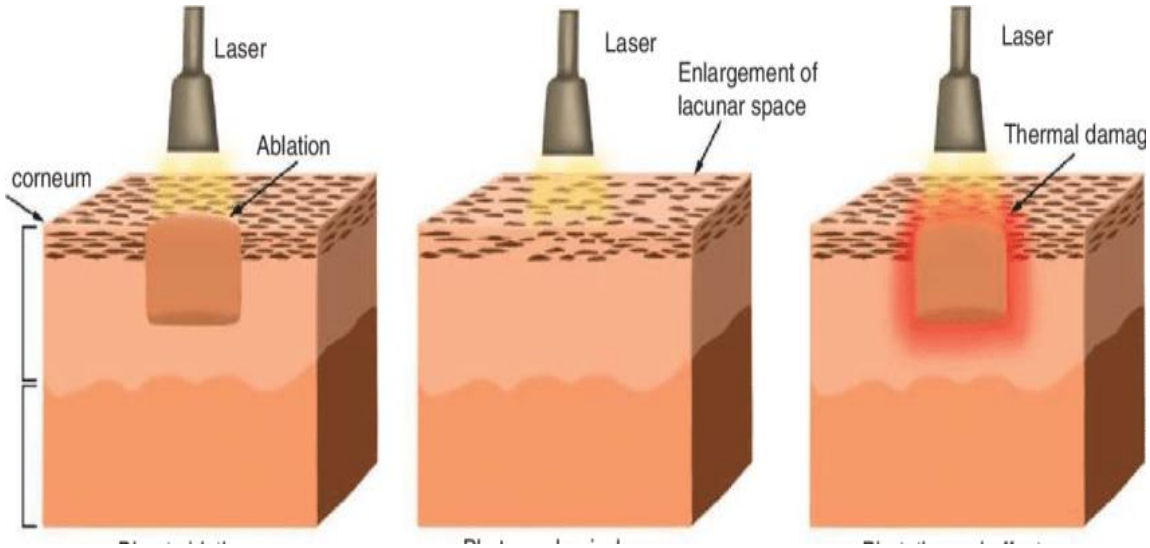

Fig. 2. Drug permeation mechanism enhanced by laser

TYPES OF LASER

Ruby Laser

The ruby laser emits a 694-nm wavelength of laser light. It is used for treating freckles, pigmented skin lesions, tattoo removal, lentigos and melasma, in clinical dermatology. [11] Ruby is a three energy level laser system. After absorbing light photons of wavelength 5500 Å from xenon flash lamp, some of the Cr3+ ions at ground energy level E1 get excited to higher energy level E3. At this energy level, they are unstable and by losing a part of their energy to the crystal lattice, they fall to the metastable energy level E2, whose lifetime is much longer (about 10-30 s). Therefore, the number of Cr3+ ions goes on increasing in E2 state while the number of these ions in ground state E2 goes on decreasing due to pumping by the flash lamp and soon the population inversion is achieved between states E2 and E1.[14]

Er:YAG Laser

Erbium YAG (Er:YAG) lasers are solid-state lasers whose lasing medium is erbium-doped yttrium aluminium garnet (Er:Y3Al5O12).The triply ionised erbium dopant (a substance added in minute amounts to another pure substance to alter its conductivity) typically replaces a small fraction of the yttrium ions in the host crystal structure, since the two ions are of similar size.The erbium provides the laser activity in the crystal.[15].

The Er:YAGlaser emits a wavelength of 2940 nm , which is efficiently absorbed by water molecules. Because of its shallow irradiation into the skin, this laser can precisely ablate the Stratum Corneum with reduced thermal injury (Figure 3). The benefits of the Er:YAG laser for ablation are quicker healing time, less erythema and fewer pigmentation problems [11].

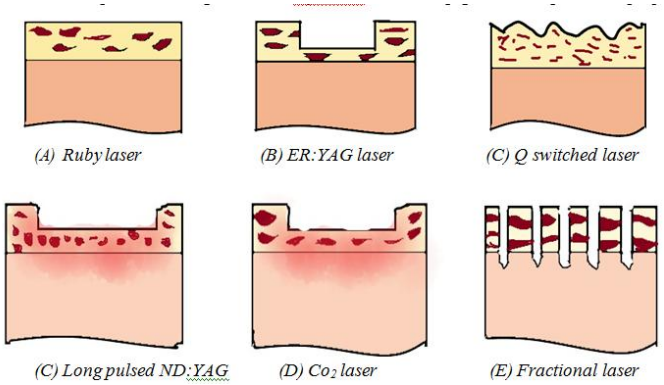

Fig. 3. Different types of laser

Nd:YAG Laser

Nd:YAG (neodymium-doped yttrium aluminum garnet; Nd:Y3Al5O12) is a crystal that is used as a lasing medium for solid-state lasers. The dopant, triply ionized neodymium, Nd(III), typically replaces a small fraction (1%) of the yttrium ions in the host crystal structure of the yttrium aluminum garnet (YAG), since the two ions are of similar size. It is the neodymium ion which provides the lasing activity in the crystal, in the same fashion as red chromium ion in ruby lasers.[17] Nd:YAG laser has a wavelength of 1064 nm and has the capability to reach deeper layers of skin tissue than other types of lasers. In Q-switched mode, Nd:YAG produces 2 wavelengths, one in thebeam of 532 nm wavelength which is useful for superficial skin lesions. Q- switching refers tothe technique of making the laser produce a high-intensity beam in very short pulses. Lasers work by emitting a wavelength of high energy light, which when focusedon a certain skin condition will create heat and destroy diseased cells. [16]

CO2 Laser

The CO2 laser has an emission wavelength of 10,600 nm, where the major chromophore is water. The CO2 laser creates instant heating of water, resulting in tissue vaporization (Figure 3). This residual thermal effect yields coagulationof skin and necrosis. The CO2 laser generally ablates less skin thickness than the Er:YAG laser at the same emittance. On the other hand, this thermal effect can rejuvenate the skin for cosmetic purposes after optimizing the feasible laser energies. The ability of the Er:YAG and CO2 lasers to promote skin diffusion of vitamin C was examined.[11]A single pass of 1.4 J/cm2 from the CO2 laser was clearly sufficient to increase the transport of vitamin C (8.2- fold), although the enhancement was lower than that by the Er:YAG laser. This indicates the negligible influence of thermolysis by the lasers on drug- permeation enhancement [15].

Fractional Laser

Fractional laser treatment is a non-invasive treatment that uses a device to deliver a laser beam divided into thousands of microscopic treatment zones that target a fraction of the skin at a time, analogous to a photographic image being enhanced or altered pixel by pixel.[18]Coagulated tissue in the treatment area stimulates a natural healing process that results in fast growth of healthy new tissue [19]. Fractional lasertreatment has bridged the gap between the ablative and non-ablative

laser techniques used to treat sun-damaged and ageing skin. While ablative laser treatments work mainly on the epidermis (surface skin cells) and non-ablative treatments work solely on dermal collagen (mid-layer of skin) only, fractional laser treatment works at both the epidermal and dermal layers of the skin.[18]Laser resurfacing can be used to treat: Fine wrinkles,Agespots,Uneven skin tone or texture,Sun-damaged skin,Mildto moderate acne scars[20]

BENEFITS

Lasers are more precise than traditional surgical instruments, and cuts can be made shorter and shallower which causes less damage to the tissue [21]. An appropriate laser treatment can effectively snap off thedark spots away. An ideal choice of expert aesthetic specialists goes with the application of ruby lasers for such issue, but many other laser and light therapy options are also available [22]. Long lasting permanent result is probably the biggest benefit of laser skin treatment. Your results fromlaser therapy are not all temporary. The resurfacing procedure shows impressive results will not fade away overnight and are long-lasting, unlike other skincare solutions. You have new skin cells but the scars, blemishes of your old skin will not reappear. It doesn't mean that your skin willnot age. Although your skin will age, it won't revert back to what it looked like once [26].

DRAWBACKS

Epidermal Laser therapy has some risks. It includes:

1) bleeding
2) infection
3) pain
4) scarring
5) changes in skin color [23]

When stronger ablative lasers that involve a longer downtime are used, there is a higher risk of developing more serious side effects. This can be mitigated by practising good pre-treatment and post-treatmentcare, as well as exploring non-ablative laser alternatives where possible. Having saidthat, side effects can also be minimized while achieving a longer-lasting outcome in the care of someone with experience [24].

CONCLUSION

The major processes that improved skin permeability were stratum corneum ablation and photothermal waves. Several laser modalities can be used to improve topical and transdermal medication delivery. Because of their ablative action on the superficial skin layers, Er: YAG

and CO2 lasers are the most commonly utilised modalities for laser-assisted medication administration. Because it causes less discomfort and has a quicker recovery period than the complete ablative laser, the fractional laser has lately been employed to promote medication absorption through the skin. Intercellular and follicular penetration are the primary mechanisms for laser-mediated delivery. The potential benefits of laser-assisted permeation include a less intrusive approach to delivering macromolecules like proteins, vaccinations, and genes as compared to parenteral injection. This possible laser use provides a novel therapy with substantial effectiveness via topical or transdermal administration. This therapy technique merits additional investigation in order to enhance its advantages.

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