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PLGA Nanoparticles Based Non-Invasive Method for Treating Dermatological Diseases

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Abstract

The aim of this study is to develop a novel cutaneous delivery technology that can create micro-sized channels to transport nanospheres within the top layer of skin for localized and systematic nanoparticulate therapeutics delivery using microneedle device, to produce sustained release and produce a localized effect which will lead to effective treatment of a variety of life-threating dermatological conditions. The skin is a natural barrier against particle permeation for topical delivery. However, it also offers a potential approach for delivery through transdermal route using microneedle. Capsaicin loaded Poly (lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) may be useful in reduction of localized pain and itch associated with various ailments and treating dermatological diseases.

Keywords

Poly (lactic-co-glycolic acid) Nanoparticles, Skin disorders

Introduction

Skin conditions and disorders are currently on the rise and affects millions of individuals across the world. They have historically been mostly brought on by either infectious infections or inflammatory conditions, both of which present difficult problems. Skin-related illnesses cover a wide range of conditions with severity ranging from benign to life-threatening. According to scientific evidence, dermatologic conditions often affect populations in many underdeveloped nations and are quite acute. There seems to be a considerable need among healthcare professionals for more attention to be paid to skin illnesses, even though these issues have not received much attention from a global audience [1]. Despite significant advancements in dermatological therapies, several of these disorders are still challenging to treat because of the patient's underlying medical issues as well as the integrity of the skin layers and their structures [2].Chronic inflammatory skin conditions like psoriasis, atopic dermatitis, and allergic contact dermatitis are brought on by inflammatory T cell infiltration, increased cytokine generation in the lesions, aberrant epidermal functional immunological dysregulation [3].

According to studies, the most effective treatment for skin disorders entails prompt diagnosis, estimation, and management of the causative agent, suitability for an effective course of treatment, that requires drug administration through the best route and the most effective schedule [2]. With the rise of new technology and significant improvements in our understanding of skin biology over the past few decades, physical and chemical methods to penetrate the stratum corneum, the skin's natural barrier, have been developed. By applying mechanical,

electrical, thermal, or magnetic energy to rupture the skin barrier, the physical approaches make it possible to transfer drugs across the skin. On the other hand, the skin barrier is momentarily weakened by the chemical techniques, which rely on chemical formulations, like gels, cutaneous solutions, patches, and ointments [3]. The first transdermal patch was approved by the United States Food and Drug Administration in the 1970s, when scopolamine was developed as a motion sickness remedy. The development of nanotechnology has opened new possibilities and concepts. We can accomplish controlled release, increase skin penetration, and improve drug stability and biodistribution by manufacturing medications in nanomaterials. Due to recent advancements in molecular biology and the expansion of the biotechnology industry, therapeutics have progressed from various small molecules to a variety of other agents, such as peptides, proteins, and nucleic acids [4]. This has been augmented by improvements in pharmaceutical formulation methods and the development of numerous nanoparticle-based systems that tends to improve the active medications in cellular and subcellular targeting, stability, and toxicity profiles. However, the therapeutic efficacy of novel NPs formulations to effectively deliver the active drugs is essentially linked to the formulation's ability to travel to its target tissue.

Skin architecture and barrier function

The stratum corneum (SC), the topmost layer of this tissue, has the innate ability to act as a barrier to the invasion of microbes and the admission of exogenous substances [3]. Essentially, the skin is made up of three layers: the epidermis, dermis, and subcutaneous layer [5]. It is the biggest organ in the body, with a 1.5 m^2 area in adults. With a thickness of 10 to 40 "μm", SC is the top layer and serves as a main physical barrier against infections, dehydration, chemical stress, and mechanical strain. About 10 to 20 layers of dead corneocyte cells, organized in a way so that the layers lie parallel to the skin surface, making up SC layers [3]. These layers always under continuous renewal and loss through cell replication and desquamation, skin peeling (Abd et al., 2016) [6]. One of the skin's primary roles is to act as a physical barrier between the body and the outside world, keeping microorganisms away. The immune system of the skin provides protection from the outside environment. In addition to providing physical defense, the skin's defense mechanism also provides immunological, metabolic, and UV protection [7]. When designing new ports of entry for therapeutic substances like active agents, medicines, and vaccines, it can be very helpful to fully understand and utilize the mechanism that confers the barrier qualities [2].

Conventional approach

Most conventional topical treatments aim to deliver the medicine for a local area, as compared to a systemic circulation. Traditional techniques are supposed to be effective on the outer surface of the skin. Common tropical skin care treatments calls for the application of creams or ointments formulation on the skin. Drugs from these preparations separate as soon as they are applied to the skin, forming a intense coating of the active substance that is quickly absorbed [8]. Moreover, stickiness and greasiness can make it difficult for patients to comply with the use of topical medications. The delivery system here demands high concentration of the formulation to work more efficiently, as it lacks the systematic release of the bioagent. Other drawbacks include allergic reactions and skin irritation, uncontrolled evaporation of the active agent and unpleasant odor. The delivery seems to be often unspecific and skin penetration is usually extremely poor with substantial variance, and their delivery is frequently non-specific. Two parameters must be imperative for the drug to be effective; the drugs must effectively penetrate the intended place in a significant volume and remain there for a defined period of time [9]. The skin is the outermost part that can be accessed for drug application, however this does not guarantee that the drug has an easy entry to the site of requirement. To overcome this, use of penetration enhancers like dimethyl sulfoxide or propylene glycol were used to increase the transport rates [10]. The use of penetration increasers generally expedites transport over the epidermal barrier, but concerns have been raised concerning the use of these enhancers in the topical delivery of medications since they may have unpleasant or even dangerous side effects [11].

Novel nanotechnology approach for delivery

Conventional topical treatments have drawbacks and are compromised in terms of patient compliance, safety, and therapeutic efficacy, as was covered in the preceding section. Novel medication administration methods using nanotechnology has paved new possibilities of research as a solution to these problems since they can decrease such inaccurate characteristics without lowering efficacy, increase the solubility of drug/bioagent along with the NPs, biodistribution and achieved controlled release, enhancement in skin permeation [3]. Nanotechnology has also become accessible and expanded the opportunities and treatment options for skin diseases using devices like microneedles to significantly enhance the transdermal delivery across the skin. These new drug carrier system with topical dermatitis appear to offer a way to overcome the problems associated with conventional topical therapy and achieve seemingly impossible goals. There are three routes—the appendageal pathway, the intracellular (transcellular), or the intercellular—allows NPs to cross the skin. The very first approach, which uses the hair follicle route normally, relies on penetration through skin appendages. The other two routes enter the cells, but since the site serves as a reservoir for the NPs, they can be kept there for a long time before they are really absorbed [12, 13].

Materials and Methods

The epidermis, dermis, and subcutaneous tissues make up the skin. In Figure 1, we propose that the employment of a wet-etch microneedle array device can considerably improve the intra/ transdermal administration of a special PLGA and capsaicin agent. Capsaicin, a member of Capsaicin is the compound found in chili peppers that is responsible for its pungent taste [14]. It has an analgesic effect and is used to treat several conditions that cause pain, including postherpetic neuralgia, nostalgia paresthetica, brachioradial pruritus, pruritus and pruritus related to hemodialysis, aquagenic pruritus, apocrinechromhidrosis, lipodermatosclerosis, alopecia etc [14].

Role of PLGA -capsaicin

Capsaicin generates burning followed by desensitization method that could lessen its negative, encapsulation with

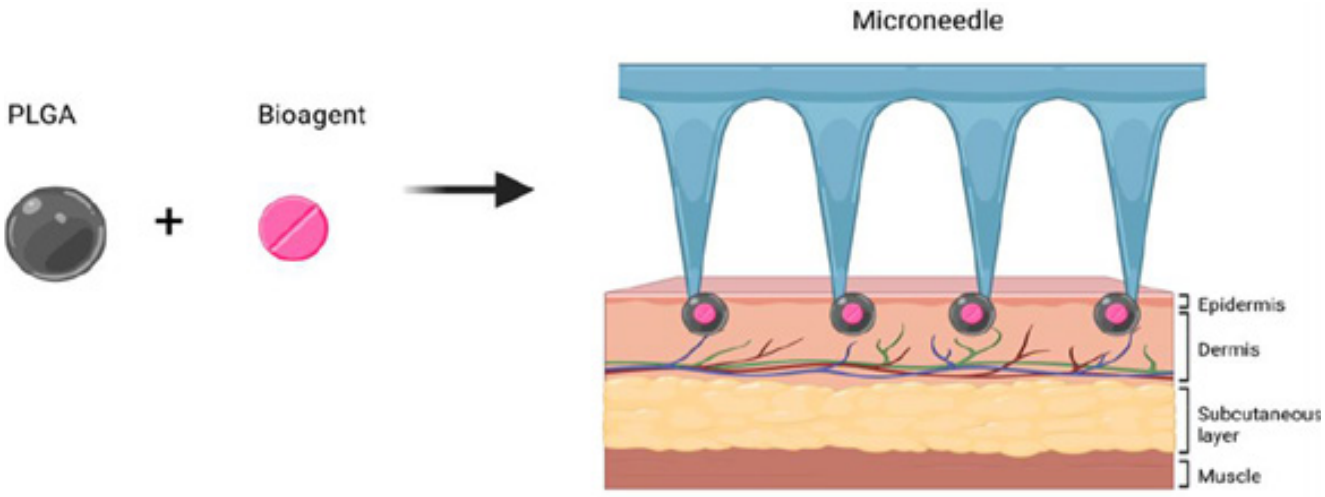

Figure 1: Systematic Transdermal delivery of polymeric nanoparticle into the skin using Micro needling technology.

PLGA NPs is one effects [15]. In atopic dermatitis, pruritis, and post-herpetic diseases, capsaicin works by activating nociceptors response against histamine to have long-lasting desensitization, cutaneous management, and neuropathic feelings. Additionally, the capsaicin-calcium-dependent activation of calmodulin and calcineurin leads to a desensitization of TRPV1 causing a diminished responsiveness of the receptor. This phenomenon evokes the analgesic effect of capsaicin [16]. This led to reducing of pain, itch associated with these skin diseases [17]. As a copolymer of PLA and PGA, PLGA NPs has distinguished itself as a significant biocompatible and non-toxic polymer with several uses in drug administration, tissue engineering, and medical and surgical equipment. The US FDA has approved PLGA for a number of medical purposes because of its biodegradability, biocompatibility, and sustained-release properties [18].

Microneedle mediated delivery of nanocarrier

Advancements in micro needling technology during the past years has shown new possible ways to inject drugs through the skin (outer corneum layer) and employ micron-sized needles to make minute channels in the outer corneum [19]. When compared to conventional transdermal delivery techniques, microneedles can transport molecules of larger sizes without disturbing the skin's nerve endings, which lessens or eliminates patient discomfort. Also, they can be used in liquid and solid formulations [20].

Figure 2 depicts the design of microneedle and its parts. Microneedle consist of three parts. The microneedle's lower portion is known as the needle base. The main cylindrical portion of the microneedle is known as the needle body. The shape of this component ensures the microneedle's reliability during skin insertion. The majority of biotherapeutics and vaccinations are administered topically via hypodermic needles. Whereas a direct method of distribution is through injection of the required nanoparticulate molecules into the body (Azmana et al., 2020) [21]. The needle tip is the only portion of the microneedle that penetrates the skin and NPs are released from the outlet openings. Various parameters, such as its length, inside diameter, and outer diameter, must

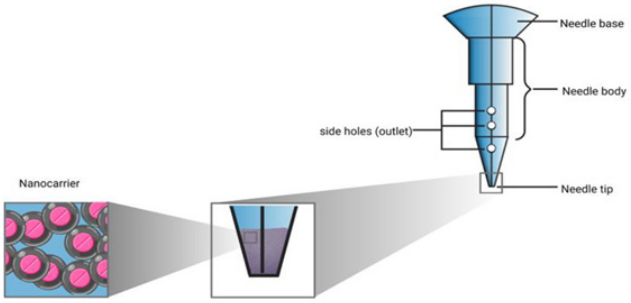

Figure 2: Design of a micro needle.

be taken into account if a desired rate of drug transportation is required. Additionally, pressure drop inside the microneedle has a significant role on the drug flow inside the lumen. The microneedle's structure has a considerable impact on the pace of medication delivery.

Conclusions

Skin disorders represent a major group of dermatologic and neurological conditions that directly cause significant health and financial burden. Skin disease are causes by various factors including inflammatory and infectious conditions. These conditions lead to disruption of skin integrity and its structures. Intensive study reveals that in order to effectively treat skin disorders, it is necessary to promptly diagnose the condition, estimate its severity, and manage it by using the most appropriate therapies. Currently, topical treatment is the most favorable choice into viable skin. Yet skin strata counteract with penetration of bioactive agent into skin, only small percent of active agent can be absorbed. The drawback associated with topical therapy is, most of them cause significant side effect to the systematic circulation and this will affect the whole body and not just skin. Microneedle technology is a device of choice for controlled transdermal delivery of drugs. Due to improved stability and reduced stress and pain, piercing the needle tip and controlling the formulation's release at a specified rate do not harm the skin's hyper elasticity. Hence it is proposed as an ideal non-invasive device for treating skin conditions. On the other hand, literature studies

revealed that using Capsaicin –PLGA NPs penetrates into the skin with much ease and had higher rate of drug delivery and detainment in the strata. This cutaneous delivery system gives the possibility of drawbacks of release rates being a reliable non-invasive delivery system for dermatological conditions, herby limiting conventional, side effects, and targeted delivery.

References

1. Sigmundsdottir H. 2010. Improving topical treatments for skin diseases. *Trends Pharmacol Sci* 31(6): 239–245. https://doi.org/10.1016/j.tips.2010.03.004
2. Gupta M, Agrawal U, Vyas SP. 2012. Nanocarrier-based topical drug delivery for the treatment of skin diseases. *Expert Opin Drug Deliv* 9(7): 783–804. https://doi.org/10.1517/17425247.2012.686490
3. Cui M, Wiraja C, Chew SWT, Xu C. 2020. Nanodelivery systems for topical management of skin disorders. *Mol Pharm* 18(2): 491–505. https://doi.org/10.1021/acs.molpharmaceut.0c00154
4. Coulman SA, Anstey A, Gateley C, Morrissey A, McLoughlin P, et al. 2009. Microneedle mediated delivery of nanoparticles into human skin. *Int J Pharm* 366(1–2): 190–200. https://doi.org/10.1016/j.ijpharm.2008.08.040
5. Paudel KS, Milewski M, Swadley CL, Brogden NK, Ghosh P, et al. 2010. Challenges and opportunities in dermal/transdermal delivery. *Ther Deliv* 1(1): 109–131. https://doi.org/10.4155/tde.10.16
6. Abd E, Yousef SA, Pastore MN, Telaprolu K, Mohammed YH, et al. 2016. Skin models for the testing of transdermal drugs. *Clin Pharmacol* 8: 63–176. https://doi.org/10.2147/CPAA.S64788
7. Roberts MS, Walters KA. 2008. Human skin morphology and dermal absorption. In: Roberts SM (ed) Dermal absorption and toxicity assessment, CRC Press, pp 1–16.
8. Nacht S, Katz M. 1990. The microsponge: a novel topical programmable delivery system. *Drugs and the Pharmaceutical Sciences* 42: 299–325.
9. Barry BW. 1987. Mode of action of penetration enhancers in human skin. *J Control Release* 6(1): 85–97. https://doi.org/10.1016/0168-3659(87)90066-6
10. Al-Japairai KAS, Mahmood MS, Almurisi SH, Venugopal JR, Hilles AR, et al. 2020. Current trends in polymer microneedle for transdermal drug delivery. *Int J Pharm* 587: 119673. https://doi.org/10.1016/j.ijpharm.2020.119673
11. Teichmann A, Heuschkel S, Jacobi U, Presse G, Neubert RHH, et al. 2007. Comparison of stratum corneum penetration and localization of a lipophilic model drug applied in an o/w microemulsion and an amphiphilic cream. *Eur J Pharm Biopharm* 67(3): 699–706. https://doi.org/10.1016/j.ejpb.2007.04.006
12. Lademann J, Richter H, Schaefer UF, Blume-Peytavi U, Teichmann A, et al. 2016. Hair follicles - a long-term reservoir for drug delivery. *Skin Pharmacol Physiol* 19(4): 232–236. https://doi.org/10.1159/000093119
13. Abdel-Hafez SM, Hathout RM, Sammour OA. 2018. Tracking the transdermal penetration pathways of optimized curcumin-loaded chitosan nanoparticles via confocal laser scanning microscopy. *Int J Biol Macromol* 108: 753–764. https://doi.org/10.1016/j.ijbiomac.2017.10.170
14. Boyd K, Shea SM, Patterson JW. 2014. The role of capsaicin in dermatology. Prog Drug Res 68: 293–306. https://doi.org/10.1007/978-3-0348-0828-6_12
15. Coulman S, Allender C, Birchall J. 2006. Microneedles and other physical methods for overcoming the stratum corneum barrier for cutaneous gene therapy. *Crit Rev Ther Drug Carrier Syst* 23(3): 205–258. https://doi.org/10.1615/critrevtherdrugcarriersyst.v23.i3.20
16. Arora V, Campbell JN, Chung MK. 2021. Fight fire with fire: Neurobiology of capsaicin-induced analgesia for chronic pain. *Pharmacol Ther* 220: 107743. https://doi.org/10.1016/j.pharmthera.2020.107743
17. Malewicz NM, Rattray Z, Oeck S, Jung S, Escamilla-Rivera V, et al. 2022. Topical capsaicin in poly(lactic-co-glycolic) acid (PLGA) nanoparticles decreases acute itch and heat pain. *Int J Mol Sci* 23(9): 5275. https://doi.org/10.3390/ijms23095275
18. Kapoor DN, Bhatia A, Kaur R, Sharma R, Kaur, G, et al. 2015. PLGA: A unique polymer for drug delivery. *Ther Deliv* 6(1): 41–58. https://doi.org/10.4155/tde.14.91
19. Saeed A, Gupta V, Goyal P, Sharif M, Pan R, et al. 2020. Annulus: a dual congestion control loop for datacenter and wan traffic aggregates. Proceedings of the Annual conference of the ACM Special Interest Group on Data Communication on the applications, technologies, architectures, and protocols for computer communication, pp 735–749. https://doi.org/10.1145/3387514.3405899
20. Cheung K, Das DB. 2016. Microneedles for drug delivery: trends and progress. *Drug Deliv* 23(7): 2338–2354. https://doi.org/10.3109/10717544.2014.986309
21. Azmana M, Mahmood S, Hilles AR, Mandal UK, Al-Japairai, KAS, et al. 2020. Transdermal drug delivery system through polymeric microneedle: a recent update. *J Drug Deliv Sci Technol* 60: 101877. https://doi.org/10.1016/j.jddst.2020.101877