Perspective in Topical Infective and Non-infective Skin Diseases Therapy with Emergence of Nanomedicine

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The human skin is constantly exposed to various microbes, viruses, pollutants, UV/other radiation and other stressors that exist in today’s life. Eventually, often we are encountered with infectious and non-infectious skin diseases such as psoriasis, acne, vitiligo, eczema, acrodermatitis, cutaneous candidiasis, athlete’s foot, cutaneous leishmaniasis and rosacea, skin cancer, etc.

The current crisis of skin infections caused by a wide range of bacteria, fungi and virus has resulted in an exponential increase in morbidity [1, 2]. Despite the recent advancements in dermatological treatments, the treatment of topical infections has always been a difficult proposition because of the lack of efficacy of existing formulations, longer period of treatment and yet incomplete recovery. Implication of various microbes like Staphylococcus aureus, Methicillin-Resistant Staphylococcus aureus (MRSA), Pseudomonas aeruginosa, Gram-positive, Gram-negative bacteria and fungi is causing complex problems [3]. Moreover, the severity of the problem also depends on the structure of skin layers and the target site. Although, the defensive properties of skin like acidic pH and significant antibacterial activity exhibited by its constituent components like Lauric acid and palmitoleic acid encompass the anti-infective mechanism against topical infections [4], however, in certain conditions like burns, wounds and diabetes mellitus, skin loses its defense mechanism with the entry of pathogens followed by the development of infection. Further, its barrier nature presents an arduous impediment for most drugs to be delivered into and through it owing to the prevailing patho-physiological conditions [5]. Besides, the drug’s intrinsic physico-chemical characteristics viz. pKa, molecular size, stability, binding affinity, solubility and partition coefficient remain unfavorable for drug delivery across the skin barrier [6-8].

Human beings are the natural hosts for many bacterial pathogens that colonize the skin as normal flora. Staphylococcus aureus and Streptococcus pyogenes account for a wide variety of bacterial infections. A wide variety of bacterial infections affect the normal physiology of skin including cellulitis, folliculitis, carbuncle and furuncle. The predisposing factors to infection include minor trauma, pre-existing skin disease, poor hygiene, and rarely, impaired host immunity. Cellulitis is a superficial bacterial infection of the lower dermis and upper subcutaneous tissue frequently affecting the legs. The major causative organism of cellulitis is Group A beta-hemolytic Staphylococcus aureus along with other microbes like Pseudomonas aeruginosa, Escherichia coli and Klebsiella species [9]. Impetigo is a superficial cutaneous infection resulting from the direct invasion of healthy tissues, or occurs secondarily to an underlying skin disease especially around nose, mouth and wounds. It occurs in patients already exposed to eczema and diabetes mainly by Staphylococcus aureus and Staphylococcus pyogenes [10]. Folliculitis is a cutaneous infection of the hair follicles such as the scalp, neck, beard area, axillae, buttocks and limbs characterized by follicular-based pustules. Carbuncles show inflamed skin and pus drainage from hair follicles [10]. The treatment strategies for bacterial skin infections include dicloxacillin, clavulanic acid, amoxicillin, erythromycin, clindamycin and vancomycin. Fungal and yeast topical infections include dermatophytosis, pityriasis versicolor and candidiasis. Dermatophytosis implies an infection caused due to Trichophyton rubrum, having high affinity for the keratinized tissue such as skin, hair and nails. The other prevalent type of fungal skin infection is caused by Candida species, namely Candida albicans. These include candida vulvovaginitis, intertrigo (skin fold infections), napkin dermatitis, chronic paronychia (nail fold infection) and onychomycosis (nail plate infection) [10]. Tinea versicolor is an opportunistic infection caused by yeast Malassezia furfur. Tinea pedis affects the feet with scaling plaques on the soles. Tinea capitis is characterized by scaly, erythematous skin with hair loss. The treatment strategies for fungal topical infections include terbinafine, clotrimazole, econazole, fluconazole, ketoconazole anditraconazole [10]. Herpes simplex (HSV), Herpes zoster, Molluscum contagiosum, Erythema infectiosum, Roseola infantum, Herpes simplex and chicken pox are some of the viral topical infections. HSV infection is painful and characterized by grouped vesicles along with dermatitis. HSV I is associated with orofacial disease and HSV II with genital infection [10]. Molluscum contagiosum spreads by the direct contact and is caused by benign pox virus. Herpes zoster (shingles) is an acute, painful dermatitis in the presence of immunosuppression. The common treatment strategies for viral infections include acyclovir, valacyclovir and imiquimod.

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The oral route of drug delivery for the treatment of topical infectious disorders suffers from various adverse reactions including hepatic toxicity, serious skin events such as drug-drug interactions resulting from metabolism through the cytochrome P450 system [10]. The topical route is the most preferred one owing to the delivery of drug molecules to the SC or epidermis and they retain there for a sufficient period of time to exert therapeutic effects [10]. The skin, although an ideal site for drug delivery, is also a major hurdle to this process. Happily, the barrier nature of the skin and more so in diseased state, presents an arduous impediment for most drugs to be delivered into and through it, owing to the prevailing patho-physiological conditions [10]. Effective anti-infective drug therapies must therefore administer and deliver the required quantity of drug into or through the skin. The drug molecule should be effectively localized in the epidermis/dermis and provide sustained release of drug over an extended period of time [10]. The skin retention of the drug molecules is also a difficult task to achieve because of the poor permeability through skin.

The application of nanotechnology to medicine, entitled nanomedicine, has significantly brightened the future of pharmaceutical and biotechnology industry in the past decade [2-3]. Nanomedicines have shown good prospective in the treatment of topical infections [10]. Topical formulations based on conventional strategies such as creams and ointments have failed to achieve active skin targeting and controlled release for the treatment of topical infections. Nanomedicine overcomes this challenge of conventional drug delivery systems based on the development and fabrication of nanostructures [10]. Various types of nanoparticulate systems have been tried as potential drug delivery systems, containing polymeric nanoparticles, liposomes, ethosomes, nanocapsules, nanogels, Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) [10-13]. The use of silver nanoparticles as drug delivery vehicles for topical infections suggests a new and promising model in the design of effective therapeutics against many pathogenic bacteria. Antimicrobial nanomedicines possess several advantages including the possibility of targeted drug delivery, overcoming the solubility or stability issues of the drug and minimize drug-induced side effects. In addition, nano-drug delivery systems have the inherent ability to overcome existing drug resistance mechanisms [10-13].

REFERENCES