

## BIOSYNTHESIS OF SILVER NANOPARTICLE FOR TOPICAL DRUG DELIVERY - POTENTIAL AND CHALLENGES

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### ABSTRACT

Transdermal drug delivery is one of the most preferred routes of administration because of its patient complaints and pharmacotherapeutic effectiveness. Present review aimed to study the possibilities of delivering herbal drug through skin by using silver nanoparticles. Herbal medicines are considered as a source of therapeutically active components with low adverse effects. Major challenge with these herbal formulations is its stability. Biosynthesis of silver nanoparticle that is synthesis of herbal formulation with silver nitrate is the one of the best way to overcome the stability problems of herbal drugs. So many marketed formulations for transdermal administration are available that containing biosynthesized nanoparticles

**KEYWORDS:** Transdermal drug delivery, Silver nanoparticles, Herbal medicines, Potentials, Challenges.

### INTRODUCTION

Silver nanoparticles have attracted increasing interest due to their chemical stability, catalytic activity, localized surface plasma resonance, and high conductivity.<sup>[9]</sup> In addition, previous reports showed that the reactive oxygen species (ROS) formed at the surface of the silver nanoparticles or by the released free silver ions under certain conditions may induce cell death of either mammalian cells or microbial cells, which provide the silver nanoparticles with unique antibacterial and antifungal effects.<sup>[10]</sup> Based on these actions, silver nanoparticles clasp great potential in preventing wound inflammation and hence promoting wound healing in the form of topical administration. For transdermal use, the skin penetration ability and safety of silver nanoparticles should be assessed.

Transdermal drug delivery (TDD) have so many benefits, but it has proven difficulties to discover a drugs that is small and lipophilic enough to permeate effectively through the skin barrier. Drugs that delivered Transdermally have better patient compliance than more painful/invasive alternative routes that require needle injection.<sup>[1-3]</sup> Other benefit of transdermal routes is the bypassing the first-pass metabolism in the liver that orally delivered drugs undergo.<sup>[1-3]</sup> Drug formulations and their concentrations can also be tuned to allow controlled release of drug into the body over long periods of time; thereby decreasing the need for multiple doses/applications.<sup>[4]</sup> Even if, few United States Food and Drug Administration (FDA)-approved transdermal drug formulations currently exist so many researchers are

attracted towards the TDDS because of this reson.<sup>[4,5]</sup> The first FDA-approved transdermally delivered drug was the scopolamine patch for motion sickness in 1979.<sup>[1,4-6]</sup> Later, a few other drugs like nicotine, fentanyl, estrogen, and testosterone have been successfully formulated into TDD systems.<sup>[5]</sup>

Currently, the research goal is to use nano technology to enhance transdermal drug systems, and to discover new methods to allow skin permeation of larger, hydrophilic drugs once thought to be impermeable to the skin. There are many TDD systems being researched, including: microneedle injection, chemical penetration enhancers, physical barrier disruption by ultrasound or abrasion, and nanocarriers.<sup>[1,7-9]</sup>

This review will focus on silvernanoparticles, which are particles made of silver on the nanometer scale. These particles are small enough to penetrate into the viable layers of skin, and they can carry herbal drug loaded on the particle surface or in the particle core. In so many cases, silver nanoparticles allow deeper skin penetration and prolonged drug release compared to more traditional TDD systems.<sup>[10]</sup> While nanoparticle skin penetration can be limited in intact skin, these systems may be ideal for drug delivery through barrier-disrupted skin to treat diseases like psoriasis and atopic dermatitis (AD), two diseases characterized by chronic pruritic, inflammatory dermatitis and skin barrier disruption.

### Transdermal route of administration

The human skin is considered as the largest organ in the body, and it is comprised of two distinct layers named the epidermis and the dermis.<sup>[11]</sup> The important functions of skin includes : physical barrier protection, immune surveillance, thermal regulation, ultraviolet light protection, and water retention. The epidermis ie the outermost layer of skin is responsible for both physical barrier protection from exogenous insults (pathogens, micron-sized particulates, and many large, hydrophilic chemicals) and water retention.<sup>[12,13]</sup>

The permeation of drugs through the skin involves the diffusion through the epidermis through the skin appendages (hair follicles and sweat glands). These skin appendages form shunt pathways through the intact epidermis, occupying only 0.1% of the total human skin. It is known that major barrier for drug permeation the stratum corneum.

### Herbal medicines for ttds

Herbal medicines means a formulation that contain any kind of plant content that provide nutritional, cosmetic and other benefits. Herbal medicines are used either for diagnosis or treatment of diseases. The major advantages of herbs include patient tolerance and minimal side effects. Also the cost of thee herbal dugs are much less compared to the synthetic ones. On the other hand, in case of sudden and serious illness the modern medicines are more effective than herbal medicines. Self-treatment is another risk factor of the herbal treatment. Moreover, lack of proper directions over doses may leads to over doses. Usage of herbs without proper identification may leads to poisoning. As the plant products are not properly regulated, customers may be cheated with inferior quality products.

**Table 1: Examples for transdermal delivery of herbal medicines.**

Pharmacological effects	Phytochemicals
Analgesic and anti-inflammatory	Capsaicin, colchicine, curcumin, catechin
Skin repair	Camptothecin derivatives
Antitumor	Bufalin, podophyllotoxin
Psoriasis and antifungal	Psoralen, harmaline
Anti-oxidant activity	Cinnamic acid, pomgranate

### Silver nanoparticles

Nanotechnology is a branch of science which is always investigated for its biomedical applications. Nanoparticles are classified broadly into two i) inorganic and ii) organic. Inorganic nanoparticles incorporate semiconductor nanoparticles like ZnO, metallic nanoparticles Ag or magnetic nanoparticles like Co: while organic nanoparticle includes carbon nanoparticles. Among these silver and gold nanoparticles attract more researches because of its superior characteristics and flexibility.

### Skin penetration of silvernanoparticles

Delivery of silver nano carriers through skin has attracted more research interest due to the antimicrobial activity of silver ion. The major advantage of TDDS is the dug ids delivered directly in to the site. But the matter of concern is that skin is a semipermeable membrane, and it will not allow the passage of particles even in nanometer scale. S,Kokura et al showed that silver nanoparticles are not able to penetrate through human skin. He also found out that if the barrier function of skin was disrupted it may be possible that 0.2 % to 2% of silver nanoparticles could penetrate the skin.

Nanoparticles penetrate skin through one of these three pathways: intracellularly through corneocytes, intercellularly around corneocytes, or via dermal structures like hair follicles (Figure 1).<sup>[44]</sup> The Franz diffusion cell is the standard tool for the study of skin penetration of small molecules and particles. In most of the studies, ex vivo skin is prepared either fresh or frozen, and the skin is placed into a device with both an upper and lower chamber. The particles are loaded into the upper chamber for the experiment and after a period of time the lower chamber and the skin itself is tested for the presence of particles.

Francesca filon larese et al studied the ability if silver nanoparticles through intact and damaged skin and found out that absorption of silver through skin is minimal but it is detectable. In case of damaged skin, the absorption of silver can be enhanced by forming nanoparticles.Kenneth Maduaabuchi ezealisiji et al assessed size dependent skin penetration of silver nanoparticles and the effect of penetration enhancers on it. According to him the choice of penetration enhancers and the size of particle have very much importance on the penetration of silvernanoparticle through the skin.

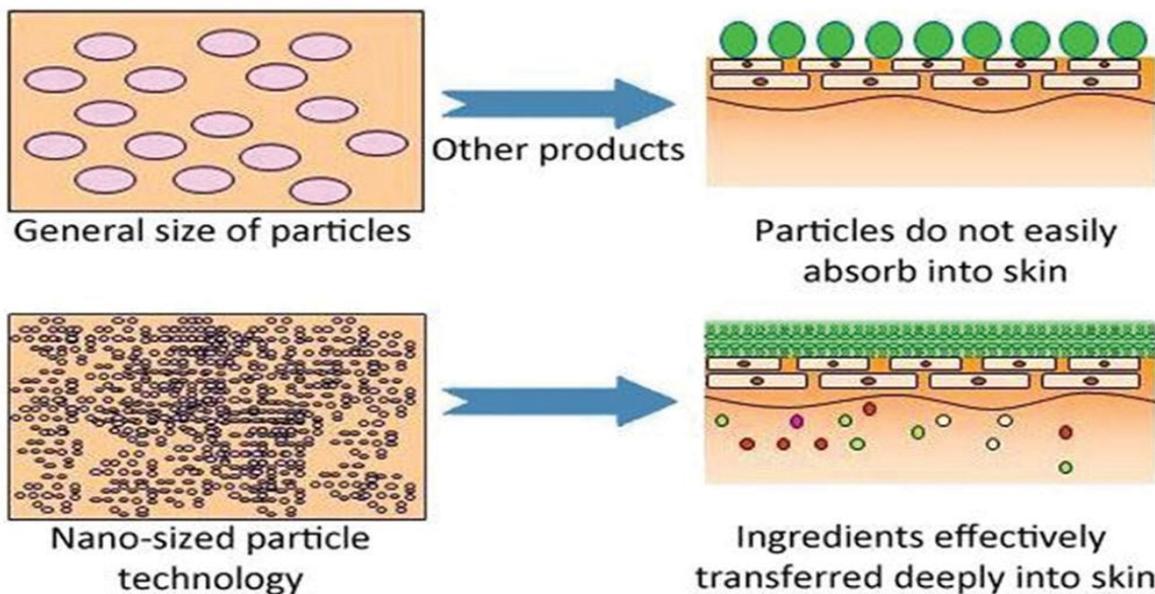


Figure 1: Transport of drug molecules through skin.

**Nano herbal formulations**

Herbal nano medicines are prepared from plant extracts or their therapeutically active constituents. Nano drug delivery systems provides better bioavailability, decreases side effects and toxicity. Some of the marketed nano herbal medicines are described as below.

**Breast cream**

St. herb nano breast cream claims that, it is a combination of “nanotechnology and the timeless Thai herb, *Pereira mirifica*”, And that niosomes expands the cellular substructure and development of the lobules and alveoli of the breasts with increased size from one to three cups [Figure 2].



Figure 2: Breast cream.

**Sunscreens**

Ultraviolet (UV) filters are developed in nano form rather than bulk form to formulate the sunscreen transparent rather than white. It is also claimed that they are more efficient when used in nanoform. SLN can act as a physical UV blocker and are able to improve the UV protection [Figure 3].



Figure 3: Sunscreen lotion

**DISCUSSION**

Transdermal drug delivery are researched for many applications, because of following reasons, delivery through skin is less painful than injection, bypasses first pass metabolism in the liver, and can be formulated for slow and constant release of drug into systemic circulation. However, healthy skin forms a physical barrier to xenobiotic chemicals and particulates. Silver nanoparticles are preferred for the transdermal drug delivery because of its antimicrobial activity. Herbal medicines mostly researched due its non-toxicity, low irritancy and easy availability. The major disadvantage of herbal medicines is of lack of stability and permeability to skin. These problems can be overcome by formulation the herbal drug in a silver nanocarrier ie the biosynthesis of silver nanoparticles to enhance the therapeutical performance of herbal medicines.

This review is based on so many research articles were the performance of biosynthesized evaluated at different levels. Annika vogt et al studied interaction of dermatologically relevant nanoparticles with skin cells

and skin, Here the interaction of silica, titanium dioxide and silver nanoparticles were studied and found that penetration of biologically relevant amount of drug occur at the site of barrier dysfunction. Ying-chen cheg et al studied transdermal delivery system of natural product.

## CONCLUSION

Nanotechnology is rapidly growing and potentially beneficial field with tremendous implication for industry, medicine, and cosmetics. The combination of nanotechnology with traditional herbal medicine may contribute a very useful tool in designing future herbal medicine with improved bioavailability profile and less toxicity. The connection between plant sciences and nanotechnology has the potential to develop an attractive symbiosis between green revolution and nanotechnology with realistic prospects for minimizing the application and generation of toxic chemicals that destroy living organisms.

## Future prospects and opportunities in india

Nanotechnology offers various modern applications in NDDSs that potentially improve the diagnosis, treatment and help to monitor of post-administration transformation of drug composition within the body systems.[28] Another important milestone to be mentioned here is computer aided drug design, which offers a lot of scope for the development of this kind of novel and advanced systems, helps in designing and developing the drugs and delivery systems consuming less time and resources with more accuracy and quality compared to traditional methods.[29-31]

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