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Delivery of Analeptics via Painless Transdermal Patches

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Abstract

Putting into service a preliminary transdermal patch on the skin, an appropriate dosage of drug can be delivered to the site of therapeutic effect within the body. This supreme delivery system is painless and more efficacious. These patches are designed by adhering analeptic compounds over them. In conjugation to these therapeutic compounds essential oils having anti-inflammatory, anticancer, antioxidant and healing properties are also used, increasing the durability of drug. Natural and synthetic polymers comprising cellulose derivatives and polyvinyl chloride respectively are significant in their designing. There are assorted categories of transdermal drugs, depending on the layers of therapeutic compounds, inclusive of single layer, bi-layer, multilayer, matrix and reservoir. Transdermal delivery has its own wondrous aptness. It enhances bioavailability of drugs eliminating the first pass effect in gastrointestinal tract. It is efficient in treating not only extraneous skin infection, but it also holds a strong curable impact on internal disorders extending from hormonal imbalance to either neurodegenerative diseases or cardiovascular diseases. Nicotine patches are prodigiously practiced treating nicotine addicts.

***Keywords*:** Drug delivery; transdermal patches; types of transdermal drugs; applications of TDD.

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1. Introduction

An expedient dosage of drug can be dispatched to the locality of analeptic effect within the body by employing a precocious patch on the skin; this is called transdermal drug delivery [1]. It is not only used to cure the injured areas but also for other treatments like hypertension, hormonal imbalance etc. This is a sort of painless treatment i.e. no ligand is bound to the pain receptors. The absorption of drug in this kind of treatment depends on many parameters like the nature of skin, the compound attached on the patch and the environmental conditions like humidity. Several experiments are conducted to examine the absorption of these active therapeutic compounds through human skin, human skin is found to be the best skin type for it. Different chemical compounds are used for designing these patches [2]. Along with these compounds essential oils are also used. These oils portray provision of anticancer, healing, anti-inflammatory and antioxidant properties. They are also used as preservative because they enhance long lasting ability of drug on the patch. So somehow such natural compounds are more important as compared to the artificially formulated chemical compounds [3]. Different polymers are used for designing transdermal patches like natural polymers including cellulose derivatives, synthetic elastomers including nitrile, hydrin rubber and synthetic polymers including epoxy, polyvinyl chloride.

There are varied types of transdermal drugs. These types are single layer, bi-layer, multilayer, matrix, reservoir and vapors. In single layer type, only one layer of drug is applied over the patch e.g. fentalyl patch designed for the cancer pain treatment. In bi-layer type, double layer of drug is filmed e.g. silicone patch which is used for the treatment of scars [4, 5]. In multilayer, polyelectrolytes are used, e.g. layer by liposomes are arranged over the patch for continues supply of drug. In matrix type, the therapeutic drug is used along with synthetic polymers[6]. In reservoir type, simvastatin is used. In vapor type methadone is used. Pharmacokinetics and pharmacodynamics are evaluated in each type. The most important benefit of it is that there is no first pass effect of drugs and an equal level of drug is maintained within the plasma flow. There are no interactions between the drug and the food, so it prevents the difficulties of drug to be absorbed in the gastrointestinal tract. In other words there is no side effect if the patient is suffering from diarrhea and vomiting issues[7, 8]. The applications of TPs are extended from skin allergies to hormonal, neurodegenerative and cardiovascular diseases and hypertension also. These therapeutic TPs are experimentally supported on model organisms.

TPs are conventionally considered for the healing purposes while in real they have huge therapeutic properties. In this piece of writing these therapeutic characteristics are enlightened defining the composition, categories and aptness of TPs.

2. Categories of Transdermal Patches

TPs are categorized depending upon the number and arrangement of layers of analeptics. The single layer adhesive drug is the simplest and the mostly used method. In this single layer drug adhesion, the upper or the adhesive layer serve as the adhesion layer to the skin and it also release the drugs. The drug in the first layer depends upon the concentration of the drug in the patch [9]. Double layer patches are used for the treatment of scars silicon is filmed over the patches in double layers. Water vapor and oxygen are required for its absorption into the body. The polymer elastomers are used as a carrier of drug [5].

In multilayer transdermal patches, the electrolytes are coated which enhances the efficiency of patches and the stability of therapeutic agents. 10 layers of liposomes are filmed. Then these liposomes are given positive and negative charges by using different cationic and anionic species. And as a result, a complex which is to be spherical is synthesized. There will be the electrostatic interactions found to be working there [7]. The layer of the matrix is made up of the semisolid matrix which contains the drug solution. The matrix transdermal patches considered as transdermal curing agent for hypertension, chronic treatment and heart failure [6].

In the reservoir type transdermal drug, the rate controlling membrane is very important because it is responsible for controlling the delivery of the drug. It follows the zero-order kinetics. This is designed to dispatch the drug at an appropriate constant rate at least for 48 h [8]. All these categories are listed in figure 1.

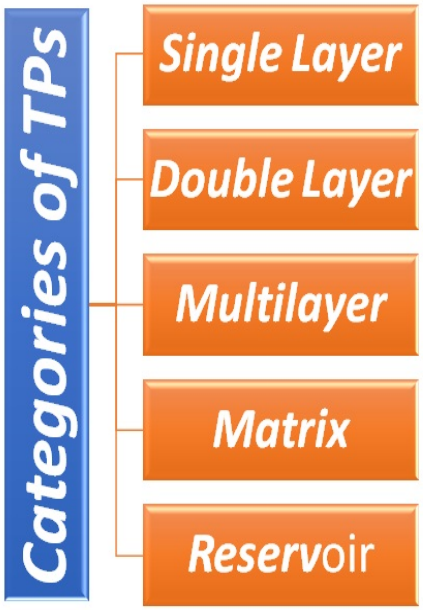

Figure 1: The transdermal patches categories

3. Aptness of Transdermal Patches

The administration of medication through a transdermal drug delivery system (TDDS) has several practical considerations which are demonstrated in figure 2. TDDS has several advantages as compared to other systems of drug delivery [10]. Difficulties in absorption of drug in the stomach and the intestine like pH change, activity of enzyme and interaction of drug with food, drinks and other drugs administered orally, can be avoided by transdermal patches. In case of vomiting and diarrhea when the oral delivery of drugs is unsuitable, these TPs can be employed. This will help to evade first pass effect. This increases the bioavailability with a single application, improving the effect of drug therapy [11]. Clinical scrutiny of TDDS involves the proper cutting and composition of TPs [10].

Skin problems like acne and allergic dermatitis are so worrying. Acne is a persistent infection of pilosebaceous units. They contain hair, sebaceous glands along with follicular canal lined with squamous epithelium.

Pilosebaceous units are more concentrated and active on the top of the face [12]. While Allergic contact dermatitis takes place in the outermost layer, stratum corneum. TPs have stupendous significance in treating these two. Morin (pentahydroxyflavone) obtained from the natural products possessing anti-inflammatory properties are transdermal delivered neutralizing allergic responses. Morin phospholipid complex (MPC) is prepared and then loaded in Carbopol 940 hydrogel (MPC-gel), which increases the flux of Morin situated on the in vitro skin penetration. To enhance penetration, different contents of penetration enhancers were dissolve into the gel and then it is screened. Then it is applied onto the mouse skin, MPC-gel results into contraction of ear blister in 2, 4-dinitrofluorobenzene (DNFB)-instigated allergic contact dermatitis (ACD).Then different cytokines levels are determined, and , histopathological analysis and T lymphocytes proliferation demonstrate that MPC is potent enough to decrease the inflammatory response which interferes in the DNFB in the mice model [13].

Neonatal infections (bacterial infections) are a supreme cause of childhood death. Polymeric microneedles are designed to deliver gentamicin. These microneedles are composed of two FDA approved polymers i.e. vinylpyrrolidone and sodium hyaluronate and gentamicin (30% w/w). they have high penetration and high mechanical strength. These are tested on animal models [14].

Several medications are available that act transdermally in CNS. These medications incorporate methylphenidate (MPH), cholinesterase inhibitors, dopamine agonists and monoamine oxidase inhibitors (MAOIs) for attention-deficit hyperactivity disorder, dementia, Parkinson’s disease and depression respectively [15]. The most prevailing neurodegenerative disorder is Alzheimer's disease. Dimethyl fumarate has potential cure for this disease. Instead of taking it orally it is more feasible to administer it through skin. However, its delivery through transdermal route requires some enhancers being coated on the patches along with it [16].

Hormonal imbalance consequences serious health issues including retarded growth, diabetes, poor reproduction and breast cancer as well. In case of children, TPs are more convenient to deliver hormones necessary for their growth, the most significant hormone delivery is of growth hormone across the skin barrier in an appropriate concentration [17]. Gelatine (Gel) and hydroxyapatite (Hap) are used to make the microneedles which are bioceramic composite having very good mechanical features. Diabetic rats act as model animals, after administrating these microneedles through transdermal injection the insulin could be detached from the composite to reduce the level of glucose in the body [18]. To overcome the pain issues, these bioceramic microneedles are replaced by the biodegradable ones by using calcium sulfate along with the gelatine. These are referred as transdermal patches. By applying these patches on the skin the diabetic patients can be treated and they can enjoy a balanced level of glucose [19]. In 1980’s the use of transdermal patches sticking testosterone over them were introduced in the market. Testosterone has property to permeate in the body through skin. It has been found an easiest way for the administration of this hormone into the body, to maintain a significant amount of this hormone in the males [20]. In US, for birth control methods, such transdermal patches are being in practice on which ethinylestradiol and norelgestromin are built in. This treatment is done once in a week in three consecutive weeks. This treatment is alternative to the oral treatment on daily basis. In Europe, these patches modified possessing gestodene instead of norelgestromin are used for this purpose [21]. Tamoxifen transdermal patches are designed for inhibiting the breast cancer. Liposomes having cationic nature are used as carriers for

tamoxifen. For experimentation xenografted mice were selected. Due to its efficient penetration power it is being used at clinical level [22].

Taking hormones orally increases the risks of cardiovascular diseases so this therapy in discouraged strictly. To get the estrogen from transdermal drug delivery system is proved to be healthy and ineffective to increase the risks of cardiovascular diseases like myocardial infection [23]. As hypertension is the life-threatening disorder, it requires a long-time treatment. Clonidine is used as anti-hypertensive drug delivered in to the body through transdermal system [24].

Nicotine patches are customarily in practice to reduce the nicotine addiction in those persons who smoke loads of cigarette about twenty a day. In combination therapy, varenicline is also accounted along with these patches [25, 26].

Figure 2: Aptness of Transdermal Patches accounting different health disorders

4. Future Perspective

Future studies may be directed towards treating more diseases. Attempts must be done to replace the painful vaccination through injections by designing such transdermal patches coated with the vaccines. This would be very effective way for vaccination of infants.

5. Conclusion

There are several systems for drug delivery, but transdermal drug delivery system is found to the most advanced, efficient and painless system. It delivers the therapeutic drugs of high efficacy and bioavailability to the targeted site within the body. The drugs to be coated on the patches must have a higher skin penetration power to eliminate the disorder at rapid speeds. Allergic reactions on the skin are treated by using such patches.

However, they have immense role in treating and preventing, the hormonal, neurodegenerative and cardiovascular diseases.

6. Abbreviations

Transdermal drug delivery system (TDDS), Transdermal patches (TPs), Morin phospholipid complex (MPC), 2, 4-dinitrofluorobenzene (DNFB), allergic contact dermatitis (ACD), Central Nervous System (CNS).

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