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Review Article

Current Trends and Recent Development of Transdermal Drug Delivery System TDDS

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A B S T R A C T

The basic goal of TDDS is to administer medications at a predefined pace into systemic circulation through the skin with little inter- and intrapatient variance. TDDS come in a variety of forms, including reservoir and matrix systems, single-layer drugs in adhesive, and multi-layer drugs in adhesive. With more than 35 items already authorised for sale in the US and around 16 active components authorised for use as TDDSs internationally, the market value of TDDS products is growing quickly. Due to its low likelihood of patient rejection, simplicity of administration, and patients' convenience and perseverance, a transdermal drug delivery system [TDDS] is a desirable substitute for traditional needle injections. However, transdermal administration is complicated and constrained by the physicochemical characteristics of the skin. The many types of TDDS approaches that are now accessible are covered in this study, along with their individual benefits and drawbacks, characterization techniques, and potential. A transdermal patch is an tenacious medical patch that's applied to the skin to administer a particular quantum of drug via the skin and into the bloodstream, constantly accelerating the mending of a damaged body part. Transdermal medicine administration is a fairly new technology that has the implicit to reduce the need for needles when furnishing a wide range of specifics, but the cost is an essential element to take into account.

Keywords

Transdermal Drug delivery system, Novel Drug Delivery system, Nanocarriers, PE,Epidermis, Skin, Drug Permeation etc.

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INTRODUCTION

Thousands of years have passed since mortal cultures used compounds on the skin as aesthetic and therapeutic agents. Still, it wasn't until the twentieth century that the skin was employed as a channel for drug administration. [1] A transdermal medication delivery system, often called a transdermal patch or skin patch, is a drug delivery method that provides a particular remedy to the systemic rotation. It's a tough region that has been treated. When delivering systemic products through the mortal skin, morphological, biophysical, and physicochemical components of the skin must be considered. [2] The Scopolamine transdermal patch(first transdermal patch authorised by the FDA in 1981) administration systems(TransdermScop, ALZACorp.) are used to avoid stir sickness, while Nitro- glycerine transdermal administration systems(Transderm Nitro) are used to treat angina pectoris associated with coronary roadway complaint. [3] The delivery of coloured medicinal compounds has been significantly impacted by TDDS, notably in the treatment of cardiovascular and central nervous system illnesses, hormone therapy, and pain management. Since TDDS avoids the gastrointestinal tract, first-pass metabolism is avoided, and medications can be delivered without being hampered by pH, enzymes, or intestinal microorganisms. Furthermore, TDDS may be utilised to manage drug release based on operational constraints, contributing to the system's excellent

continuity. Utmost significantly, because TDDS is a non-invasive administration fashion with no discomfort or strain on the case, medicines may be safely and fluently handed to youths or the senior. It still does not use its full eventuality because of the hardwired skin barricade. [4,5]

Route of Drug penetration and Anatomy of Skin.

The skin, which has several layers and is the body's outermost organ, serves to shield us from external dangers including chemicals, heat, and toxins. [6] The dermis, which contains blood vessels and produces skin cells, and the epidermis, which serves as protection, are the two layers that make up this skin. There are chemicals in each layer that prevent transdermal distribution. [7,8] The transepidermal and transappendegeal channels, which are diagrammatically shown in Figure below, are the two likely pathways for drug penetration across unbroken skin. The stratum corneum, a multi-layered barrier with a sophisticated architectural design, is one barrier that molecules must traverse on their way along the transepidermal pathway. Inter- or intracellular transepidermal penetration are the two categories.[9]

Corneocytes, which are Keratinocytes that have reached their terminal differentiation, are capable of transporting hydrophilic or polar solutes intracellularly. Moving through intercellular spaces enables the diffusion of non-polar or lipophilic solutes within the continuous lipid matrix. Molecules travelling through the transappendegeal route cross across hair follicles and sweat glands. [10]

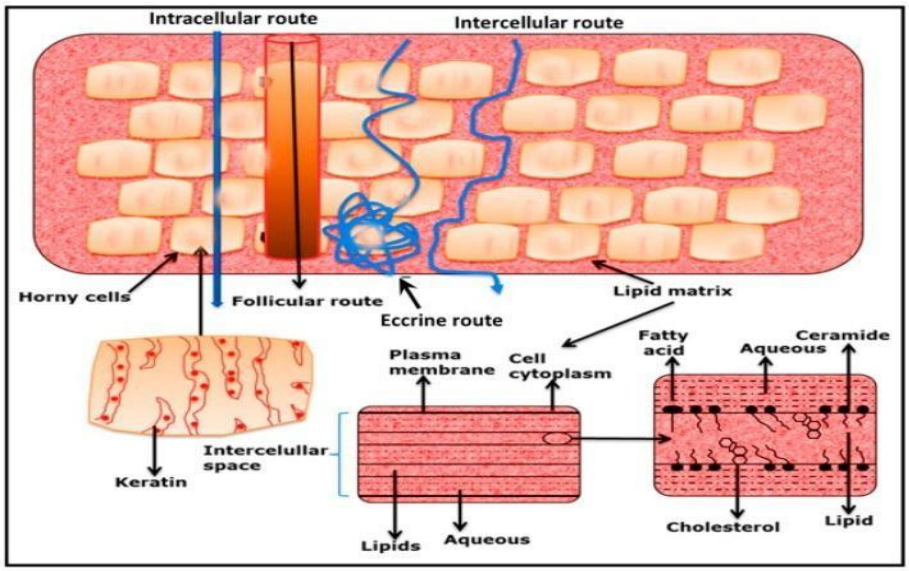

Figure 1: Anatomy of skin

Elements of Transdermal Patch

Table 1: Elements of Transdermal Patch with their description and functions. [11-13]

S. No.	Element	Description and Functions	Examples
1.	**Liner**	The patches are safeguarded while being stored. It needs to be taken out before usage.	Silicone, Fluorosilicone etc.
2.	**Drug**	The drug solution and release liner are in direct contact.	Nicotine, Nitroglycerine etc.
3.	**Adhesive**	Along with sticking the patch to the skin, it acts to bind the patch's components together.	Acrylic, polyisobutylene [PIB], and silicone etc.
4.	**Membrane**	It controls the release of the drug from the Reservoir and multi-layer patches.	Chitosan,Polyhydoxyethyl methacrylate etc.
5.	**Backing**	The film isolates the patch itself from the environment outside.	Natural polymers.
6.	**Polymer**	The medication's release from the device is controlled by a polymer matrix that is created by dispersing the drug in an appropriate polymer.	Xanthan gum, Sodium alginate, Chitosan, HPMC etc.

ADVANTAGES & DISADVANTAGES OF TDDS.

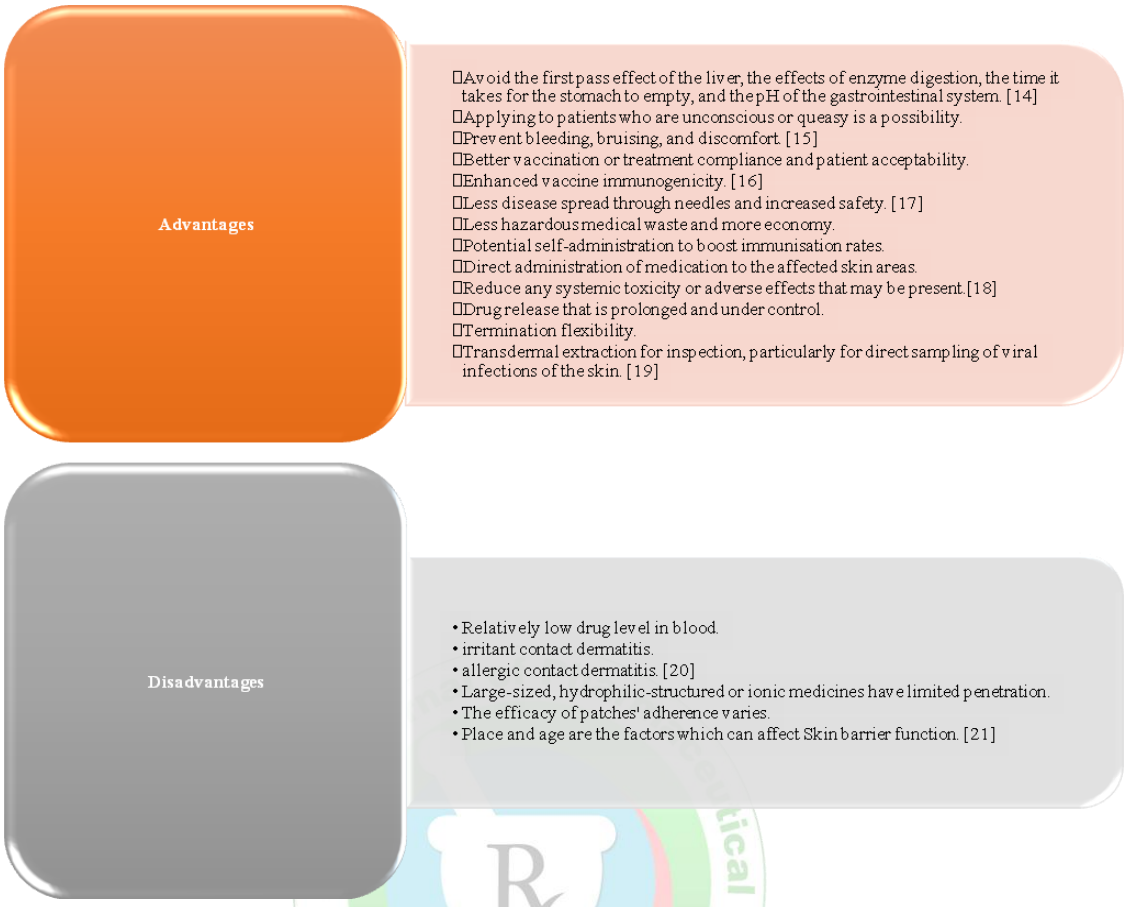

Figure 2: Advantages and Disadvantages of TDDS. [22-24]

STRATEGIES FOR PENETRATION PROMOTION

Passive promotion

The use of penetration enhancers [PE] and the use of nanocarriers to deliver medications into the skin are the two most often used passive approaches to increase skin permeability.[25] PE may improve molecules' solubility and diffusion in the skin, allowing molecules to permeate the skin [26] The primary process may include PE's destruction of the corneal cell capsule as well as its interactions with intracellular keratin, SC's composition, and the partition coefficient between lipid bilayers. [27-28]

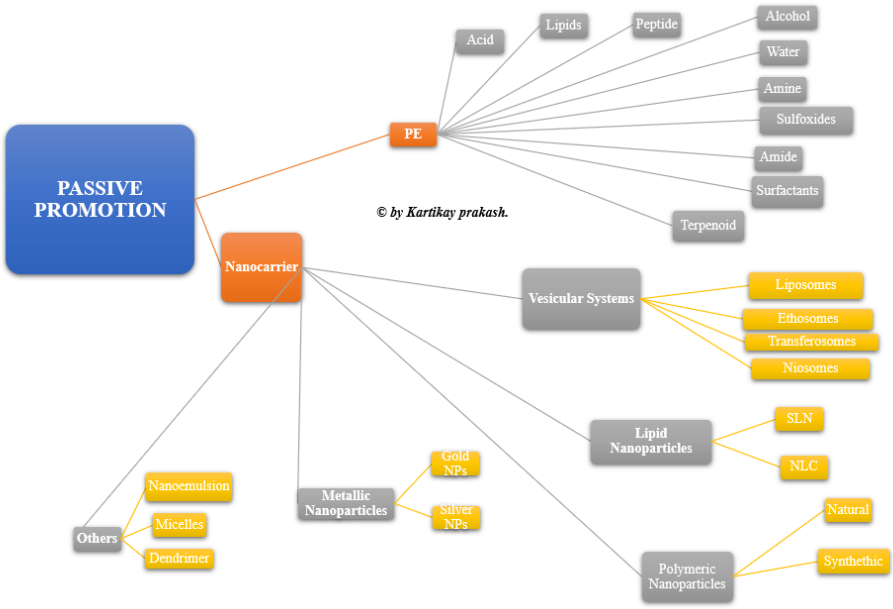

Figure 3: Passive Promotion

PE often irritate the skin, which greatly restricts their use in medicine [29] Embedded medications can also enter the skin using nanocarriers. They have been demonstrated to be beneficial in the treatment of cancer, hair loss, infections, and other conditions. [30]

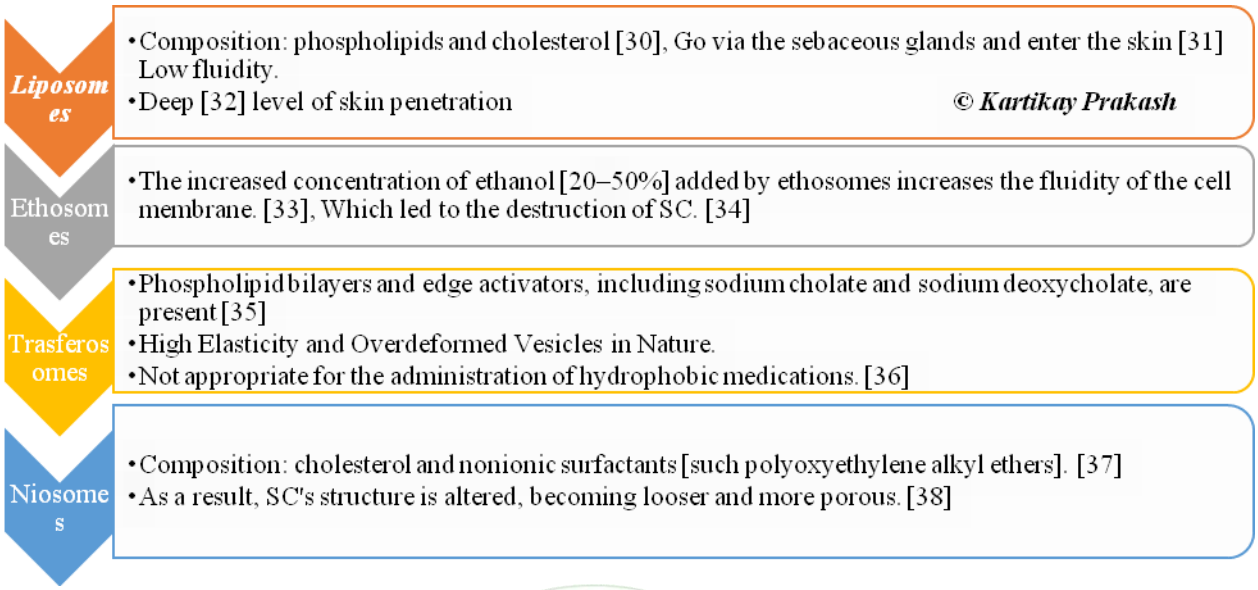

Figure 4: Examples of Passive promotion

Active promotion

Among the active techniques for skin permeabilization are ultrasound, mechanical techniques like microneedling [MN] and tape stripping, electrically assisted microneedles [electroporation and iontophoresis], velocity-based tools [powder injection, jet injectors], thermal approaches [lasers and radio-frequency heating], and velocity-based devices. [39] A greater variety of drugs may now be delivered through the skin thanks to these techniques. Active procedures either use external energy to drive the transportation of medicine through the skin or physically harm the stratum corneum. [40] Active techniques, as opposed to passive ones, also offer more repeatable control over drug distribution patterns, removing delays between injection and medication reaching systemic circulation.[41,42]

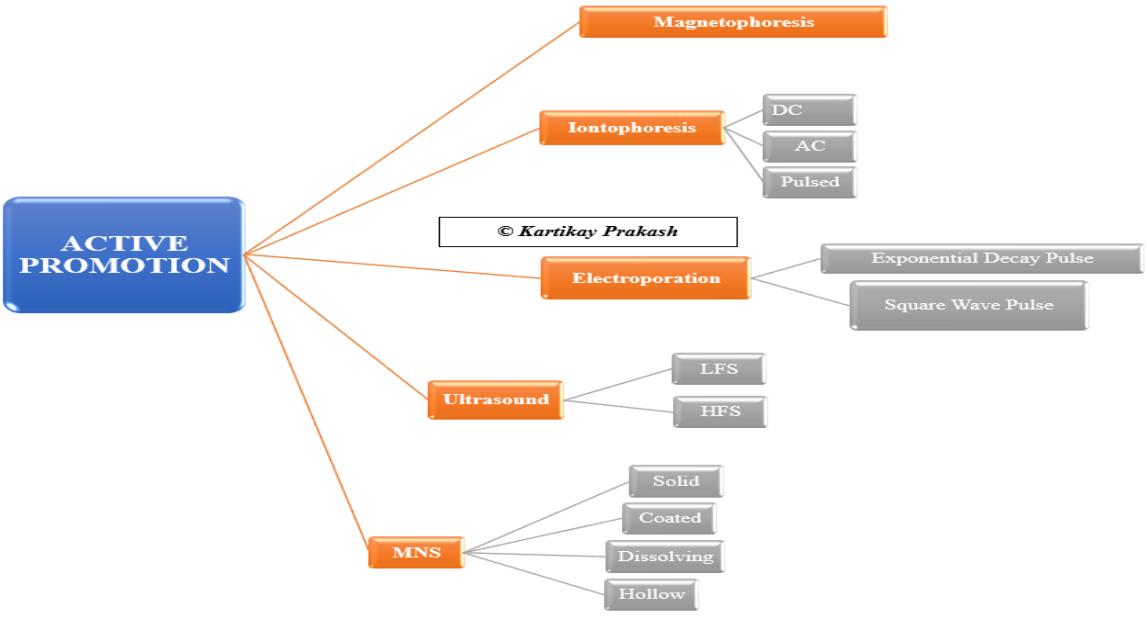

Figure 5: Active promotion

Some of these active methodologies will be described below.

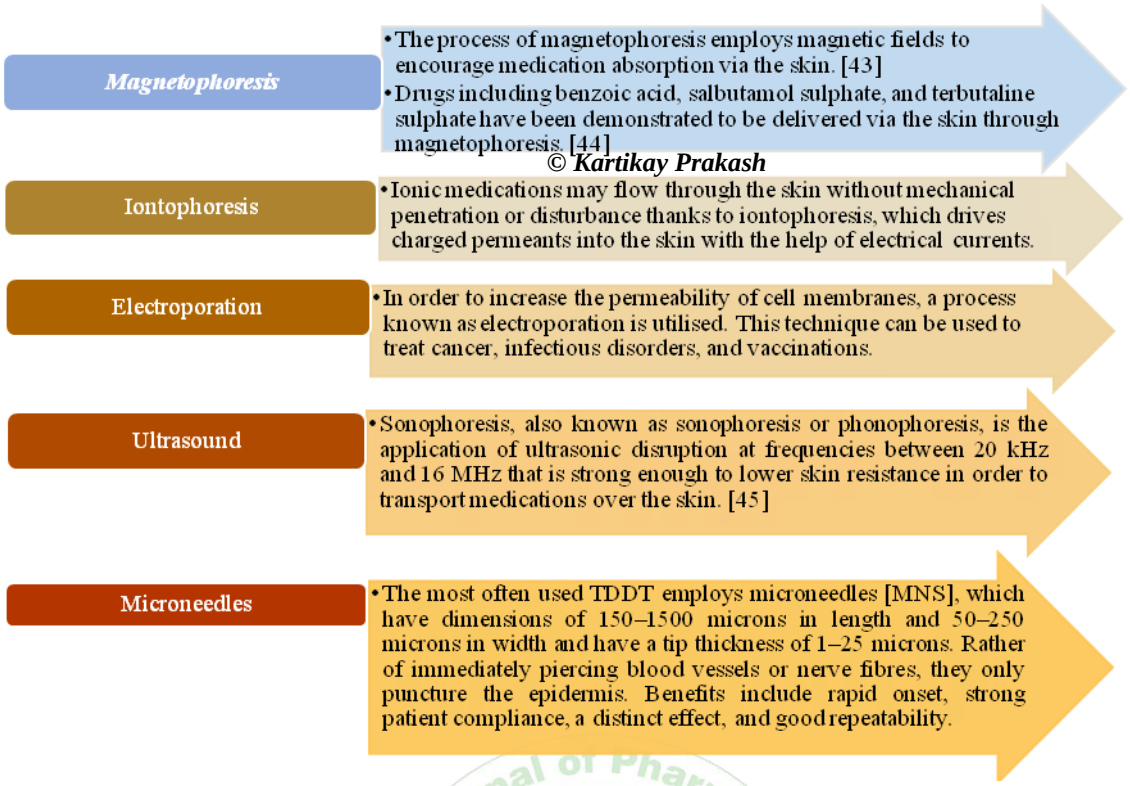

Figure 6: Examples of Active Promotion Methodologies. [46-50]

DISEASE CURED/TREAT VIA TRANSDERMAL ROUTE

Herpes simplex

Herpes labialis and vaginal herpes are the most prevalent varieties of herpes simplex, which is brought on by the herpes simplex virus. The type 1 and type 2 herpes simplex viruses are what cause cold sores, also known as herpes labialis, although genital herpes more frequently affects the vaginal region than HSV-1. [51,52]

Varicella and herpes zoster

Varicella and herpes zoster are brought on by primary VZV infection, and they are both caused by VZV. Patients with impaired immune systems are more likely to experience consequences such hepatitis, myelitis, cranial nerve palsies, meningitis, pneumonia, and widespread infection. [53-57]

Warts

Warts or verrucas are cutaneous viral infections brought on by the human papillomavirus [HPV]. They manifest as papules or plaques, which can vary in size and frequently have an abrasive, scaly surface. Skin lesions that have spread locally are rather common. Common warts [verruca vulgaris], fat warts [verruca plana], plantar and palmar warts [condyloma acuminatum], and anogenital warts [verruca vulgaris] are the four main classifications of warts based on their anatomical locations or morphologies. Treatment for warts often involves the physical destruction of infected epithelial cells or the use of immune-mediated methods. Cryotherapy, which employs liquid nitrogen to freeze and kill wart lesions, is currently the most often used method. But because cryotherapy is so painful, some patients might not be able to put up with additional treatments. [58-60]

Influenza

Influenza is a contagious respiratory disease caused by influenza viruses. The intensity of flu symptoms can range from mild ones like fever, headaches, sore throats, and runny nose to more serious ones like pneumonia that can lead to hospitalisation or even death. Immunosuppressed or elderly patients are far more likely to develop serious problems and die as a result. The influenza vaccine is the most effective way to prevent influenza and its population spread. [61-63]

Measles

The measles is a highly contagious illness that spreads through the respiratory system when aerosols or droplets are inhaled. It is still a leading cause of illness and mortality in children worldwide, despite having a safe and effective vaccine. [67-68]

COVID-19

COVID-19 is a deadly global pandemic caused by SARS-CoV-2, a new virus of the Coronavirus family. It is the seventh known Coronavirus and belongs to the genus "Beta-Coronavirus" and family "Coronaviridae". As of 15 August 2020, in India, 25, 89,208 cases, 6, 77,959 active cases, 18, 60,672 recovered cases and 50,085 deaths have been reported. [69-70]

Parkinson's disease

The neurochemical foundation of Parkinson's disease [PD] is the gradual degradation of the nigrostriatal neuron and the resulting decrease in striatal dopamine. The first evidence of a striatal dopamine deficiency in the post-mortem brains of PD patients was found in 1960, and this finding served as the impetus for the development of dopamine replacement therapy. [71-75]

Table 2: Diseases cured by TDDS and Role of TDDS in the or Management

S.NO.	DISEASE	TYPE OF TDDS	ROLE OF TDDS	REFERENCES
1.	**Herpex Simple**	• Buccal mucoadhesive patches • Moisture-activated patches • Dissolving polymeric microneedles	Drug Delivery of Acyclovir	[76-80]
2.	**Varicella and Herpes Zoster**	• Transdermal patches	Drug delivery of lidocaine for post-herpetic neuralgia	[80-86]
		• Coated microneedles with recombinant gE of VZV	VZV Vaccine	
3.	**Warts**	• Transdermal karaya gum patches	Drug delivery of salicylic acid	[87-92]
		• Solid microneedles	Facilitated penetration of topical bleomycin and 5-FU	
		• Microneedle patches	Drug delivery of bleomycin	
		• Microneedle arrays with HPV pseudovirusencapsidated Plasmids	HPV vaccine	
4.	**Influenza**	• Coated microneedles with • inactivated influenza virus	1. Influenza Vaccine	[93-99]
		• Coated microneedles with VLPs		
		• Microneedles with trimeric • Influenza Hemagglutinin protein		
		• Tip-coated [selective antigen] Microneedles		
		• Surface-modified microneedle Arrays	2. Capture circulating influenza antigen-specific IgG	
5.	**Measles**	• Coated microneedles with live attenuated measles virus	Measles Virus	[100-103]
		• Polymeric microneedles with standard measles vaccine		
		• Dissolving microneedle patches		
6.	**COVID-19**	• Microneedle based oropharyngealswabs with integrated virus-specific Antibody	Reduce False negative result of COVID-19 Testing	[103-106]
		• Dissolving microneedles • containing embedded SARS- CoV-2-S1 subunits	COVID-19 Vaccines	
7.	**Parkinson's Disease**	• Subcutaneous patch	Delivery of ND0611 carbidopa	[107,108]

CURRENT TRANSDERMAL DRUG FOR MEDICAL USE US MARKET LISTED

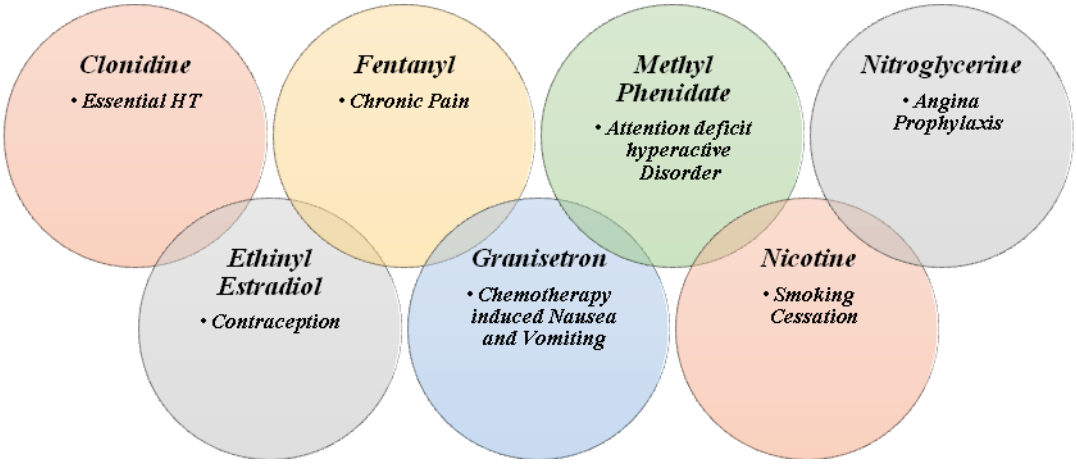

Figure 7: Current TDDS and their Medicinal uses [109-110]

CONCLUSION

TDDS technology has been a breakthrough in mass delivery, avoiding first-pass metabolism and other perceptivity associated with drug delivery routes. Microneedles can boost transdermal administration of drugs, macromolecules, or patches, but more exploration is needed to attain lesser safety, low skin damage, and cost-effectiveness. Advances in these TDDSs may help reduce the frequency of conditions, vaccination, and long-term treatment.

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