Current Therapies of Alzheimer's Disease and Future of it's Management by Using Transdermal Delivery: Tabular Update

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Abstract

The estimated 55 million people worldwide are thought to be afflicted with Alzheimer's disease (AD), and the number of new instances of the disease is rising at a rate of 10 million each year, making the situation extremely concerning for the entire world. Given that there is now no cure for neurodegenerative diseases like AD, this serves as an important reminder to improve research and treatment. The blood–brain barrier, which prevents blood–brain drug molecules from entering the brain compartment, is mostly to blame for the brain's intricate structure and the dearth of medications for treating neurodegenerative disorders. For the purpose of delivering medication molecules to the intended location in the brain, a number of innovative and traditional formulation techniques, including oral, intravenous, gene. Iontophoresis is a non-invasive technique that uses an electric field to deliver drugs locally and systemically. Diffusion of the chosen medication via the skin, mucosa, enamel, dentin, and other tissues is made possible by iontophoresis. Therapeutic compounds can be supplied 10–2000 times more efficiently than traditional methods.

Key words:- Iontophoresis, transdermal, Alzheimer's disease, blood-brain barrier, neurodegenerative disorder

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1. Introduction:

Transdermal drug transport is based on delivering drugs across the epidermis to have a long-lasting systemic effect. Researchers are interested in researching controlled zero-order absorption, simple administration mode, easy termination in the event of failure, avoiding effects of the first pass, reducing side effects, sustained drug delivery, and improved patient compliance.Since the first transdermal patch for scopolamine which was approved in 1979, numerous transdermal patches for scopolamine, nitroglycerin, nicotine, clonidine, fentanyl, estradiol, testosterone, lidocaine, and oxybutynin are in the market today. Human skin's limited permeability remains a major obstacle to its widespread therapeutic use because it requires sufficient drug permeability through the stratum corneum, developing an efficient transdermal system is a major challenge.

Additionally, it is essential to ensure that the drug delivery systems do not cause skin irritation, and the drug is administered in accordance with the desired pharmacokinetics and pharmacodynamics and is not metabolized excessively. [1]

Due to the limitations of the existing transdermal technology, this curiosity waned, and it was discovered that the number of drug candidates suitable for this route was limited. This led to the development of cutting-edge methods for improving permeation interest in transdermal delivery, such as:

- The prodrug approach
- Chemical Potential Adjustment
- Ionic complex
- Eutectic Systems
- Encapsulting in Liposomes
- High Velocity particles
- Lowering of skin resistance by chemicals
- Microneedle array
- Abrasing the Skin
- Phonophoresis, Sonophoresis
- Electroporation
- Magnetophoresis
- Damaging the Stratum corneum by Laser radiation
- Iontophoresis

There are currently more than 20 transdermal patches in the market which contain 13 drug molecules. Transdermal products containing clonidine, nicotine, and glyceryl nitrate are available in the market. Antianginal (nitroglycerine, isosorbide dinitarte), antihypertensive (Clonidine), antiemetics (Scopolamine), hormones (estradiol, testosterone), urinary antispasmodic (oxybuyrin), local anesthetic (lidocaine), and CNS drugs (fentanil, nicotine) are just a few of the many important pharmacological classes represented by this small group of commercial products. Numerous additional applications are awaiting FDA approval.[2]

The development of transdermal research has been significantly aided by the introduction of physical enhancement methods like iontophoresis and the possibility of programmed delivery. In the United States, iontophoretic products have already been introduced, heralding a new era of programmed transdermal drug delivery.[3]

ADVANTAGES [4]

Transdermal drug delivery has a number of significant benefits, including:

1. Transdermal medication delivers a drug in a steady stream for a long time.
2. It is possible to avoid the adverse effects or therapeutic failures that are frequently associated with intermittent dosing.
3. By avoiding specific problems associated with the drug, such as gastro-intestinal irritation, low absorption, decomposition due to hepatic "first-pass" effect, formation of metabolites that cause side effects, short half-life necessitating frequent dosing, etc., transdermal delivery can increase the therapeutic value of many drugs.
4. Transdermal drug administration can produce an equivalent therapeutic effect at a lower daily dose than is required for oral administration, for instance.
5. Patient compliance is improved and intra- and inter-patient variability is reduced as a result of the simplified medication regimen.
6. These systems make it possible to manage oneself.
7. The transdermal patch can be removed at any time to end the drug input.
8. Drug delivery through the skin can be used as an alternative method for patients' care delivery (unconscious or seated) who is unable tolerate oral medications.

DISADVANTAGES [4]

1. The possibility of a local irritation at the application site is one of the greatest drawbacks of transdermal drug delivery.

2. Erythema, itchiness, and local edema may be brought on by the drug, adhesive, or other excipients in the patch formulation.
3. The skin's low permeability limits the number of drugs that can be delivered via transdermal route, which is yet another significant drawback.
4. Many medications, particularly those with hydrophilic structures, penetrate the skin too slowly to be helpful.
5. The skin's barrier function varies from person to person, from person to person, and with age as well.

SELECTION OF DRUG CANDIDATES[5]

A crucial step in the success of transdermal research is selecting suitable candidates.

- Since a transdermal drug delivery system should not cover more than 50 square centimeters, it is only suitable for drugs with daily doses of less than a few milligrams.
- The drug should have a low effective concentration, probably around one nanogram per milliliter.
- The medication ought to have a short half life ($t^{1/2}$).
- The transdermal route can be helpful for special patients, such as preterm infants, but it may not offer any additional benefits for common patients for drugs with a very long biological half-life.
- Skin toxicity should not be caused by the active ingredients.
- A drug with a low molecular size is preferred because the drug's ability to diffuse through polymer and skin depends on its molecular size.
- The drug's melting point should be low.
- Transdermal delivery is a good option for drugs that break down in the gastrointestinal tract or are inactivated by the hepatic first-pass effect.
- Under transdermal delivery's near-zero-order release profile, the drug must not cause tolerance.
- Transdermal delivery can also be used for drugs that need to be administered for a long time or have negative effects on non-target tissues.

CURRENT ADVANCES IN TRANSDERMAL DELIVERY OF DRUGS FOR ALZHEIMER'S DISEASE: An uneven bio distribution, a lack of drug targeting specificity, the need for large doses to achieve local concentration, and adverse side effects caused by such high doses are the main issues with oral drug delivery. Drugs for Alzheimer's disease are considered ideal Transdermal candidates due to their limited bioavailability and extensive first pass metabolism. Along with Alzheimer's, many other drugs have been used to treat diseases like hypertension, hyperglycemia etc. [6]

Various researches in this category so far done are summarized below in tabular form:

TABLE 1: CURRENT RESEARCHES IN TRANSDERMAL DELIVERY OF BIOACTIVES FOR ALZHEIMER'S DISEASE:

S.NO.	NAME OF THE RESEARCHER	WORK TITLE	FINDINGS
1.	Matthew Solan 2024	Drugs for Alzheimer's disease	Currently, the main drugs used to treat Alzheimer's are what's known as symptomatic

			therapies, meaning they ease symptoms but don't address the cause of the disease. These include cholinesterase inhibitors(donepezil, galantamine, and rivastigmine) and memantine used orally in the form of pill. Rivastigmine comes in a patch, it is often used for people who can't tolerate the pills. People with certain types of cardiac arrhythmias shouldn't take cholinesterase inhibitors, as they can slow the heart rate. A more recent entry into the field, lecanemab, may help slow the progression of the disease. [7]
2.	Letícia Basso et. al. 2024	Transdermal Therapeutic Systems for the Treatment of Alzheimer's Disease: A Patent Review	Two classes of medications are used to treat Alzheimer's disease (AD); donepezil, galantamine, and rivastigmine are acetylcholinesterase inhibitors, and memantine is a non-competitive antagonist of the N-methyl-D-aspartate receptor. Although these are typically taken orally, there are transdermal therapeutic systems (TTSs) commercially available for rivastigmine and donepezil. The transdermal route has been preferable for guardians/caregivers due to ease of use, reduced side effects, and improved adherence to therapy. [8]
3.	Astik Kumar et. al 2023	Current and Future Nano-Carrier-Based Approaches in the Treatment of Alzheimer’s Disease	Drugs that are used as cholinesterase inhibitors are discussed below. Physostigmine ,Tacrine , Rivastigmine, Donepezil, Phenserine, Galantamine , Memantine , Allopregnanolone . [9]
4.	YaojunJu et. al. 2022	Pathological mechanisms and therapeutic strategies	In Alzheimer’s disease drug development, many good

		for Alzheimer’s disease	therapeutic strategies have been investigated in clinical evaluations. However, complex mechanism of Alzheimer’s disease and the interplay among different pathological factors call for the come out of all-powerful therapies with multiple curing functions. [10]
5	Li-Kai Huang et. al. 2020	Clinical trials of new drugs for Alzheimer disease	The drugs available for AD treatment, including cholinesterase inhibitors and an antagonist of the N-methyl-D-aspartate receptor, can only inhibit dementia symptoms for a limited period of time but cannot stop or reverse disease progression. In ongoing clinical trials, researchers have developed and are testing several possible interventions aimed at various targets, including anti-amyloid and anti-tau interventions, neurotransmitter modification, anti-neuroinflammation and neuroprotection interventions, and cognitive enhancement, and interventions to relieve behavioral psychological symptoms. [11]
6	MayankSinghal et. al. 2019	Controlled Iontophoretic Delivery in Vitro and in Vivo of ARN14140-A Multitarget Compound for Alzheimer's Disease	ARN14140 is a galantamine-memantine conjugate that acts upon both cholinergic and glutamatergic pathways for better management of Alzheimer's disease. Poor oral bioavailability and pharmacokinetics meant that earlier preclinical in vivo studies employed intracerebroventricular injection to administer ARN14140 directly to the brain. Transdermal iontophoresis was able to deliver ARN14140 noninvasively to the brain.

			[12]
7.	Tomasz M. Karpinski et. al. 2018	Selected Medicines Used in Iontophoresis	Data regarding the selected medicines used in iontophoresis. Iontophoresis enables diffusion of the selected drug via skin, mucosa, enamel, dentin, and other tissues. The amount of delivered therapeutic molecules is about 10–2000 times greater than conventional forms of delivery.[13]
8.	Thuy Trang Nguyen et al 2017	Current advances in transdermal delivery of drugs for Alzheimer's disease	This article reviews the technical principles, novel techniques of transdermal delivery drug, and prospects for future development for the management of cognitive and behavioral dysfunctions in AD patients. [14]
9.	Preshita Desai et. al. 2015	Therapeutic targets and delivery challenges for Alzheimer's disease	Different drugs are used to treat AD by oral administration of rutin, mifepristone, clioquinol, estradiol, galactose. Drugs used for transdermal route are Donepezil, galantamine, huperzine A, rasageline, selegiline, memantine, Aβ(1-42) antigen. Out of these drugs the drug used for iontophoresis are donepezil, rasageline, selegiline, memantine. Current market status and ongoing clinical investigation for Alzheimer's disease therapeutics is of transdermal drug delivery of Rivastigmine.[15]
10.	Fong Yen Woo et al 2015	Formulation optimization of galantaminehydrobromide loaded gel drug reservoirs in transdermal patch for Alzheimer's disease	This optimized reservoir formulation was then fabricated in the transdermal patch system. This patch system has moderate pH, high drug content, and controlled drug-release pattern. Thus, this patch system has the potential

			to be used as the drug carrier for the treatment of Alzheimer's disease.[16]
11	Niketkumar Patel et. al. 2014	Influence of electronic and formulation variables on transdermal iontophoresis of tacrine hydrochloride	Tacrine permeation was directly proportional to tacrineconcentration upto 10 mg/ml but further increase in concentration (upto 20 mg/ml) exhibited permeation flux plateau. The results of this study show that transdermal tacrine permeation can be controlled by electronic and formulation variables which would be useful for the development of transdermal iontophoretic delivery of tacrine for the treatment of Alzheimer's disease.[17]
12	SonalSaluja 2013	A novel electronic skin patch for delivery and pharmacokinetic evaluation of donepezil following transdermal iontophoresis	Donepezil was successfully delivered iontophoretically at levels sufficient to produce pharmacodymanic effect. The amount delivered across hairless rat skin and areas under the curve (AUC) were found to rise in proportion to the current levels. Peak plasma levels of 0.094, 0.237 and 0.336µg/ml were achieved at 0.13, 0.26 and 0.39mA respectively. [18]
13	Roseanna Brady et. al. 2013	Adherence to Cholinesterase Inhibitors in Alzheimer's Disease: A Review	All three approved agents (donepezil, galantamine and rivastigmine), modest improvements in measures of disease severity last for approximately 6 months, but seldom result in recovery of lost function. , a number of studies have reported on the benefits of transdermal drug delivery of rivastigmine in patients with AD. [19]
14	Dhaval R Kalaria 2012	Comparison of the cutaneous iontophoretic delivery of rasagiline and selegiline across porcine and human skin in vitro	The results demonstrated that therapeutic amounts of rasagiline and selegiline could be easily delivered by transdermal iontophoresis with

			simple gel patches of modest surface area.[20]
15	S. del Rio-Sancho et al. 2012	Transdermal absorption of memantine – Effect of chemical enhancers, iontophoresis, and role of enhancer lipophilicity	The transdermal administration of memantine may have advantages with respect to oral therapy when treating advanced stages of Alzheimer's disease. With the ultimate objective of administrating memantine through a transdermal patch, the absorption of the drug across skin was evaluated by means of in vitro permeation studies. [21]
16	Anne Corbett et. al. 2012	Drug repositioning for Alzheimer's disease	Existing drugs for Alzheimer's disease provide symptomatic benefit for up to 12 months, but there are no approved disease-modifying therapies. Given the recent failures of various novel disease-modifying therapies in clinical trials, a complementary strategy based on repositioning drugs that are approved for other indications could be attractive [22]
17	Antonio Di Stefano et. al. 2011	Drug delivery strategies for Alzheimer's disease treatment	Conventional Alzheimer's disease (AD) therapy is based on the administration of the drugs donepezil, galantamine, rivastigmine and memantine through oral route. Transdermal drug delivery of drugs like Physostigmine, galantamine, , rivastigmine, Phenserine, tacrine, nicotine, 17β-Estradiol [23]
18	William A Banks 2011	Drug delivery to the brain in Alzheimer's disease: consideration of the blood-brain barrier	Successful treatment of Alzheimer's disease (AD) will require drugs that can negotiate the blood-brain barrier (BBB). The BBB is not simply a physical barrier, but a complex interface that is in intimate communication with the rest of

			the central nervous system (CNS) and influenced by peripheral tissues. [24]
19	Ben Seltzer 2010	Galantamine-ER for the treatment of mild-to-moderate Alzheimer's disease	An extended release form of the cholinesterase inhibitor (ChEI) drug galantamine (galantamine-ER) was developed, chiefly to increase adherence to medication regimes in patients with mild-to-moderate Alzheimer's disease [25]
20	David Prvulovic et al 2010	Galantamine for Alzheimer's disease	Galantamine can improve and stabilize cognitive performance, activities of daily living and behavioral symptoms over the course of 6 months and its efficacy and tolerability are comparable with those of other ChE inhibitors (rivastigmine and donepezil). As long as no other drug therapies with comparable or better clinical efficacy emerge, galantamine will remain one of the standard first-line medications for mild-to-moderate AD. [26]
21	Kate McKeage 2010	Spotlight on memantine in moderate to severe Alzheimer's disease	The combination of memantine plus donepezil was dominant to donepezil therapy alone in regard to QALYs gained when treatment periods exceeded 1 year in patients with moderate to severe disease. Thus, in the management of patients with moderate to severe Alzheimer's disease, memantine provides an effective treatment option. To date, clinical trial support is greater for memantine use in combination with an AChE inhibitor, while more data are needed to confirm its efficacy as monotherapy. [27]
22	Jun Ming Wang et al 2010	Allopregnanolone reverses neurogenic and	APalpha reversed the cognitive deficits to restore learning and

		cognitive deficits in mouse model of Alzheimer's disease	memory performance to the level of normal non-Tg mice. In 3xTgAD mice, APalpha-induced survival of neural progenitors was significantly correlated with APalpha-induced memory performance. These findings suggest that early neurogenic deficits, which were evident before immunodetectableAbeta, may contribute to the cognitive phenotype of AD, and that APalpha could serve as a regenerative therapeutic to prevent or delay neurogenic and cognitive deficits associated with mild cognitive impairment and Alzheimer's disease. [28]
23	Cristina Grossi et. al. 2009	Clioquinol Decreases Amyloid-beta Burden and Reduces Working Memory Impairment in a Transgenic Mouse Model of Alzheimer's Disease	Clioquinol (CQ) is a “metal protein attenuating compound” that crosses the blood-brain barrier and binds, with high affinity, copper(II) and zinc(II), two metal ions critically involved in amyloid-βaggregation and toxicity. CQ was recently proposed for the treatment of Alzheimer’s disease, but controversial data have been reported so far concerning its real therapeutic advantages.[29]
24	Fernanda G De Felice et. al. 2009	Protection of synapses against Alzheimer's-linked toxins: insulin signaling prevents the pathogenic binding of Abeta oligomers	Synapse deterioration underlying severe memory loss in early Alzheimer's disease (AD) is thought to be caused by soluble amyloid beta (Abeta) oligomers. Mechanistically, soluble Abeta oligomers, also referred to as Abeta-derived diffusible ligands (ADDLs), act as highly specific pathogenic ligands, binding to sites localized at particular synapses [30]

25	Agnes L F Chan 2008	Transdermal delivery of treatment for Alzheimer's disease: development, clinical performance and future prospects	Transdermal drug delivery systems have been developed to deliver phenserine, rivastigmine, nicotine and estradiol for the management of cognitive and behavioural dysfunctions in patients with Alzheimer's disease because this form of administration has several advantages, including maintenance of sustained therapeutic plasma concentrations of drugs, easy application and reduced systemic adverse effects.[31]
26	Jiri Patocka et. al. 2008	Possible role of hydroxylated metabolites of tacrine in drug toxicity and therapy of Alzheimer's disease	Tacrine belongs to the group of acetylcholinesterse (AChE) inhibitors used as drugs for treatment of Alzheimer's disease (AD). The hepatotoxicity of tacrine was observed only in the part of persons and why not every patient with AD responds to the treatment by this drug. [32]
27	Darryl Potyk et. al. 2005	Treatments for Alzheimer disease	There is good evidence that cholinesterase inhibitors and memantine are modestly effective in the treatment of AD. Cholinesterase inhibitors appear to be effective throughout the spectrum of AD, while memantine, alone or in combination with cholinesterase inhibitors, is effective in late stage disease.[33]
28	Rashmi S Upasani, Ajay K Banga 2004	Response surface methodology to investigate the iontophoretic delivery of tacrine hydrochloride	Iontophoresis was used to deliver tacrineHCl across rat skin. Experiments were performed according to Box-Behnken design to evaluate effects of drug concentration (X1), current density (X2), and donor buffer molarity (X3) on cumulative drug delivered in 24 h (Y1), 6 h (Y2), iontophoretic flux (Y3), and post-iontophoretic flux

			(Y4).[34]
29	M S Parihar, TarunaHemnani 2004	Alzheimer's disease pathogenesis and therapeutic interventions	A direct understanding of the molecular mechanism of protein aggregation and its effects on neuronal cell death could open new therapeutic approaches. Some of the therapeutic approaches that have progressed to the clinical arena are the use of acetylcholinesterase inhibitors, nerve growth factors, nonsteroidal inflammatory drugs, estrogen and the compounds such as antioxidants, neuronal calcium channel blockers or antiapoptotic agents.[35]
30	Christopher M Clark , Jason H T Karlawish 2003	Alzheimer disease: current concepts and emerging diagnostic and therapeutic strategies	Alzheimer disease is a genetically complex disorder. Emerging diagnostic methods that are based on biochemical and imaging biomarkers of disease-specific pathology hold the potential for accurately diagnosing Alzheimer disease at the earliest stage of the illness--the time when disease-modifying treatment will be most effective. Currently available cholinesterase inhibition therapy targets the cognitive symptoms. [36]
31	WojciechDanysz , Chris G Parsons 2003	The NMDA receptor antagonist memantine as a symptomatological and neuroprotective treatment for Alzheimer's disease: preclinical evidence	If overactivation of NMDA receptors is present in AD, memantine would be expected to improve both symptoms (cognition) and to slow down disease progression because it takes over the physiological function of magnesium. [37]
32	Mohammad Hossain et. al. 2002	Estimation of the absolute bioavailability of rivastigmine in patients with mild to moderate dementia of the Alzheimer's type	Bioavailability of orally administered rivastigmine, an approved therapy for patients with mild to moderate dementia of the Alzheimer's type, at the highest approved single dose of 6 mg. [38]

34	Sean Lilienfeld 2002	Galantamine--a novel cholinergic drug with a unique dual mode of action for the treatment of patients with Alzheimer's disease	Galantaminehydrobromide is a tertiary alkaloid drug that has been developed and approved in a number of countries including the USA and several countries in Europe as a treatment for mild-to-moderate Alzheimer's disease (AD). Galantamine has a unique, dual mode of action. It is a reversible, competitive inhibitor of acetylcholinesterase (AChE), and is the only drug actively marketed for the treatment of AD with proven activity as an allosteric modulator of nicotinic acetylcholine receptors (nAChRs). [39]
35	B P Imbimbo et. al. 2001	Pharmacodynamic-tolerability relationships of cholinesterase inhibitors for Alzheimer's disease	Numerous cholinesterase inhibitors have been investigated for treatment of this disease, the rationale being to support the cholinergic system by blocking the degradation of acetylcholine released from presynaptic neurons. These drugs can be classified as reversible (tacrine, donepezil and galantamine), pseudo-reversible (physostigmine, eptastigmine and rivastigmine) or irreversible (metrifonate) enzyme inhibitors. [40]
36	R H Guy et. al. 2000	Iontophoresis: electrorepulsion and electroosmosis	the roles of electrorepulsion and electroosmosis have been reconsidered from a simple theoretical point of view, and experimental approaches by which their relative importance may be estimated have been proposed and subjected to initial evaluation. [41]
37	T Jaskari et al 2000	Controlled transdermal iontophoresis by ion-exchange fiber	heiontophoretic flux enhancement of sodium salicylate from the fiber was substantial. As the drug has to be released from the ion-

			exchange fiber before permeating across the skin, a clear reduction in the drug fluxes from the cationic and anionic fibers were observed compared to the respective fluxes of the drugs in solution. Overall, the ion-exchange fibers act as a drug reservoir, controlling the release and iontophoretic transdermal delivery of the drug. [42]
38	L J Scott, K L Goa 2000	Galantamine: a review of its use in Alzheimer's disease	Acetylcholinesterase (AChE) inhibitors are the most promising class of drugs for the treatment of Alzheimer's disease (AD). Galantamine is a reversible, competitive, tertiary alkaloid AChE inhibitor. The drug is selective for AChE rather than butyrylcholinesterase. Adverse events associated with galantamine are mainly cholinergic, usually mild to moderate in intensity and transient. Galantamine has been evaluated in several large well-designed studies and, given the relative lack of established treatment options, it may be considered as one of the first-line pharmacological treatments in patients with mild to moderate AD. [43]
39	K Walter et. al. 1995	Pharmacokinetics of physostigmine in man following a single application of a transdermal system.	A single application of the physostigmine patch over 24 h produced detectable plasma drug concentrations after a mean lag-time of 4 h. Thereafter, the drug was absorbed continuously from the PTS and putative therapeutic plasma concentrations were measured over approximately 18 h. A mean absolute bioavailability of 36% was determined for the transdermal system and 3% for

			the oral solution. The mean amount of physostigmine released from the transdermal system after 24 h was 5.7 mg. Because of extensive metabolism, only 2.2 mg of physostigmine were detected systemically.[44]
40	Drora Levy et. al. 1986	A Novel Transdermal Therapeutic System as a Potential Treatment for Alzheimer's Disease	Clinical improvement in AD might be expected from drugs which elevate cholinergic activity in the brain. These drugs include centrally active acetylcholinesterase inhibitors such as physostigmine and direct acting agonists such as arecoline and oxotremorine administered parenterally or bethanechol infused intracerebroventricularly. Some of these drugs as exemplified by physostigmine, have a short biological half-life and a narrow therapeutic index, which limit their clinical application. [45]

2. Conclusion

In the arena of global development, everyone is racing to improvethemselves, leading to various chronic diseases, as well as neurodegenerative disorderssuch as AD. Developing the right drugs is a challenging task for researchersdue to the complicated etiology of Alzheimer's disease.Iontophoresis is a precious and non-invasive method, which can be used for topical treatment of pain, inflammation, infections and cancers. Some drugs, for example, lignocaine or sodium Fluoride is already administered by iontophoresis to patients. Other drugs are in in-vitro studies or have been tested on animals, and further research is needed on a range of drugs. The efficacy of non-ionic drug delivery using this method in particular is warranted.Various active compounds and treatments like cholinesterase inhibitors, NMDA, vaccine, and alkaloid from herbal medicine are being studied for their effectiveness in treating neurological disorders when administered in transdermal form. The enhanced permeability of these substances through the skin was shown in lab experiments and in living organisms, with their effectiveness and reduced side effects being highlighted as strong evidence for the benefits of this method of drug administration. Different transdermal drug delivery methods are discussed, such as the use of appropriate formulations, carriers, and enhancers for penetration. The success of the Rivastigmine patch presents possibilities for creating comparable formulations for AD patients.

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