Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

Bioactive-Loaded Transdermal Drug Delivery Systems: A Promising Approach for Neurodegenerative Disease Therapy

Sanjay. B.M[1], Akiladevi. D[2*], Snehan. D[3], Jaiganesh. S[4]

[1,3,4]Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies, Pallavaram, Chennai-600117.

[2*]Professor and Head, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies, Pallavaram, Chennai-600117.

(Received: 25 March 2026 Revised: 30 April 2026 Accepted: 26 May 2026)

KEYWORDS

Neurodegenerative disorders, Transdermal drug delivery system (TDDS); Transdermal patches; Neuroprotective agents; Sustained drug release,

Drug bioavailability; Nanocarriers;

Microneedle-assisted delivery; Patient

compliance; Drug permeability.

ABSTRACT:

Treatment of various neurodegenerative diseases like Parkinson's disease, Alzheimer's disease, and Huntington's disease have many challenges to global health due to their progressive nature and the limited efficacy of existing pharmacological agents. Conventional oral and parenteral delivery of medications like Rivastigmine, Rotigotine, selegiline, and cannabinoids helps in improving cognitive function, motor symptoms, and behavioural problems but do not always provide desired therapeutic results, as they may undergo extensive first-pass metabolism, have varying plasma levels, and lack (Blood Brain Barrier) BBB penetration, leading to side effects during systemic administration. Hence, switching to natural based drug therapy is emerging as neuroprotective natural substances like Bacopa monneri, curcumin drug delivery system bypass first pass metabolism and reduce gastrointestinal irritation and improved patient safety and tolerability. Resveratrol, Betulinic acid, when combined with various polymers like HPMC, PVA, chitosan, and Eudragit provides enhanced bioavailability and extended drug release when compared to oral forms. Transdermal drug delivery system (TDDS), particularly the transdermal patches, can be a suitable approach for long-term treatment of neurodegenerative diseases because of their advantages providing controlled and sustained drug delivery, increased bioavailability, reduced gastrointestinal side effects, and improving patient compliance. Transdermal Patches of bioactive compounds produced as nanocarriers, microneedles are used to enhance drug transport and achieve targeted delivery to the brain, and contributes to improvements. This review critically examines the effectiveness of synthetic medications and its limitation, transdermal drug delivery of conventional drugs, and the bioactive based transdermal drug delivery systems. Natural compound–based patches offer an effective, safer, and patient-friendly approach for managing neurodegenerative diseases.

1. INTRODUCTION

The term neurodegenerative diseases (NDs) cover a broad spectrum of diseases that cause the progressive loss of the structural and functional parts of either the central nervous system (CNS) or the peripheral nervous system (PNS). Among the most common of these disorders Alzheimer's disease, Parkinson's disease affects elderly people at age of 60. **[1]**

One form of delivery employed in transdermal drug administration is the patch. Before the medication can penetrate the skin, the drug molecules must first be dissolved to generate molecules capable of permeation across the matrix **[2].** A transdermal delivery technique whereby exact medicine administration into the circulation can be achieved through the skin, the transdermal patch is the patch helps to reduce systemic side effects while increasing the therapeutic effectiveness of the medicine since it controls the release of the medication.**[3]** This approach of medicine delivery offers more regulated drug distribution than other methods like oral, intravenous, and intramuscular **[4].** One of the neurodegenerative diseases is Alzheimer's disease (AD) which is slowly deteriorating disease mostly affecting the hippocampus and the vast

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

cerebral cortex of the human brain. The illness mainly affects the elderly especially those over 65 and shows symptoms like cognitive decline, behavioural changes, and memory and psychological deficits.**[5].** Parkinson's disease (PD), another disease in this category reduces dependency and quality of life also and increasing early death risk for those affected. This condition causes major damage to dopaminergic nigrostriatal neurons, which causes impaired motor control and brought-on symptoms including bradykinesia, resting tremor **[6].** Amyotrophic lateral sclerosis (ALS) eventually leads to respiratory failure, paralysis, and finally death, the serious ND called amyotrophic lateral sclerosis (ALS) causes severe degradation and both upper and lower motor neurons death **[7].** One more disease called Huntington's disease (HD) is distinguished in the basal ganglia by an excess of dopaminergic potential and a deficit of Gamma-aminobutyric (GABA) activity. Among its clinical symptoms are unusual movements, cognitive impairments, and emotional changes **[8].**

Conventional treatments for neurodegenerative diseases depend on typical dosage forms, mostly oral and parenteral formulations. The most often used dosage forms are oral tablets, capsules, and solutions since they are cheap, easy to manage, and practical.**[9]** For Parkinson's disease, the most often prescribed treatments are levodopa and carbidopa, which raise dopamine levels; donepezil, rivastigmine, and galantamine are the cholinesterase inhibitors used to treat cognitive symptoms of Alzheimer's disease**[10].**Sublingual products, inhalation therapies, and injectable forms are also employed in some clinical situations when oral administration is not feasible or during urgent symptom management. In neurodegenerative diseases, conventional dosage form has several significant disadvantages like lesser bioavailability due to its first pass hepatic effects and leads to changes in systemic drug levels. Many neurotherapeutic drugs will disintegrate in the gastrointestinal system, are lesser able to permeate the Blood-brain barrier (BBB) and other biological membranes. Dysphagia, dementia are the compliance in the elderly and those with neurodegenerative disorders **[11].**

Among various Novel drug delivery system, Transdermal medicine delivery systems (TDDS) present a practical substitute for conventional delivery methods for neurodegenerative diseases. Bypassing the gastrointestinal tract and first-pass metabolism, transdermal patches administer medicines directly into the systemic circulation via the skin **[12].** Among its advantages are fewer gastrointestinal side effects, reduced fluctuations in plasma concentration, controlled and steady drug release, and enhanced patient compliance. Better tolerability and fewer gastrointestinal adverse effects than oral capsules have been demonstrated for rivastigmine patches, therefore they are often used in Alzheimer's disease. In Parkinson's disease, similarly, rotigotine patches are used to provide continuous dopaminergic stimulation, therefore reducing motor fluctuations and enhancing symptom management **[13].**

One step forward in transdermal medication delivery are microneedle patches. Made of biodegradable polymers, silicon, or metals, it may be designed to stay intact after insertion, dissolve, or expand **[14].** Micro needle patches have been studied for the delivery of medicines including rasagiline, rivastigmine, and natural neuroprotective chemicals which have been shown in preclinical studies to give better therapeutic outcomes, sustained release, and greater bioavailability **[15].** Another advanced technology like 3D printing is a powerful tool for personal medicine. 3D printing enhances the stability, permeability, and extended delivery of drugs by facilitating the use of biodegradable polymers, hydrogels, and nanocarriers in microneedle and patch formulations. The long-term management of neurodegenerative diseases appears to be highly promising **[16].** Although 3D printing is used in oral dose formulations, implants, and biomedical devices, its application in transdermal drug delivery is still in its infancy with only a few 3D-printed transdermal patches available in the market **[17].** However, the integration of 3D printing with transdermal systems provides new avenues for patient-specific treatment planning, customized dosing, and controlled drug release **[18].** Extended-release transdermal patches prepared by using advanced technologies can provide continuous drug delivery for weeks, months, or even years, thus obviating the need for daily drug intake **[19].**

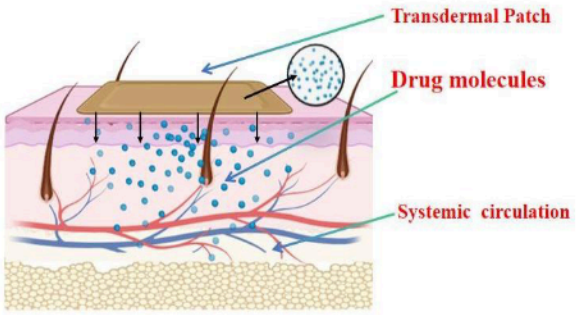
For patients with neurodegenerative disorders, these extended-release systems improve patient compliance, reduce caregiver burden. Integration of natural agents like Bacopa monneri, Curcumin, Resveratrol, Betulinic Acid, with above said modern technology like provides enhanced bioavailability and extended drug release when compared to oral forms. These patches reduce the adverse effects caused by synthetic drug delivery. Natural compound-based patches offer an effective, safer, and

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

patient-friendly approach for managing neurodegenerative diseases **[20].**

Starting with a review of neurodegenerative disorders and their typical dosage forms, this review discusses about synthetic as well natural bioactive based transdermal drug delivery techniques and their clinical importance. Further examining innovative transdermal techniques, we pay particular attention to 3D printing methods and microneedle-based systems. With a focus on the possibility of personalized and long-acting transdermal therapies to improve patient outcomes, we draw attention to future prospects and developing trends that might affect the following generation of drug delivery technologies used to treat neurodegenerative illnesses**.**

Fig1: **Mechanism of transdermal drug delivery**



2. CONVENTIONAL DOSAGE FORMS FOR NEURODEGENARATIVE DISEASES

Oral tablets and capsules are conventional and affordable for long-term therapy for managing neurodegenerative diseases. To relieve the symptoms of neurodegenerative illnesses, Levodopa is sometimes given to Parkinson's disease patients to raise dopamine levels and reduce movement symptoms. Alzheimer's patients' cognitive ability is improved by cholinesterase inhibitors like donepezil, which also help to manage the disease **[21].** Tetrabenazine is used to treat Huntington's disease and reduces chorea by depleting monoamines. Memantine, galantamine, donepezil, and Rivastigmine are used to manage Alzheimer's disease. The piperidine derivative donepezil reversibly inhibits acetylcholinesterase. Oral drugs come in either 5 mg or 10 mg dosages. Available in both oral and transdermal forms, rivastigmine has better gastrointestinal tolerability. Common doses range from 1.5 mg to 6 mg capsules **[22].** Galantamine reversibly inhibits Ache. Furthermore, it interacts with nicotinic receptors to improve cholinergic activity. Galantamine is available in immediate-release as well as extended-release forms. One of the most often prescribed medicines, memantine slows the course of Alzheimer's disease. Even though memantine helps to shield glutamatergic neurons from an overabundant and long-lasting influx of calcium into the cells, oxidative stress and neuronal apoptosis still affect them. It is available in tablets of 5 mg and 10 mg as well as capsules of 7 mg. Treatment for dementia with memantine in conjunction with donepezil involves three further medicines; Memantine hydrochloride is the other drug. Memantine is an especially potent medicine when administered in conjunction with donepezil, rivastigmine, or galantamine **[23].**

Lowering blood pressure is the primary mechanism of action of beta-adrenergic blocking medication Carvedilol, which blocks the beta-adrenoceptor and triggers vasodilation, hence leading to alpha 1-adrenoceptor blockage. The suggested dosage is 3.125 to 6.25 mg twice daily taken orally as a tablet. Due to first-pass hepatic metabolism, carvedilol has a poor bioavailability of roughly 23% and is absorbed mostly by the GI system. Bioavailability of carvedilol is low, and its half-life (6 hours) is very short. For this reason, a different path is necessary to boost bioavailability and patient adherence **[24].**

Rasagiline mesylate (RM) is a second-generation, extremely strong, selective, irreversible inhibitor of monoamine oxidase (MAO-B). It raises neurotransmitter availability at the synapse while slowing down dopamine degradation, used in the treatment of early-stage Parkinson's disease, RM has neuroprotective actions against a number of neurotoxins in addition to anti-apoptotic and antioxidant capabilities. Presently accessible in oral form, rasagiline mesylate has a somewhat limited bioavailability (~36%) and brief half-life. Many oral anti-Parkinson drugs, including Rasagiline mesylate, need to be ingested multiple times a day and are sometimes related to a treatment "off" period during which motor symptoms return between two doses and cause great discomfort to Parkinson's disease patients. Oral therapy might be challenging, especially for those in an advanced stage of Parkinson's disease, since elderly patients often have difficulty swallowing solid oral dosage formulations **[25].**

Levodopa + Carbidopa – dopaminergic precursor which improves motor symptoms. Available in tablet form in

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

combination with carbidopa to reduce peripheral metabolism. Widely used as first-line therapy**.** They improve cognition and control motor symptoms, Carbidopa inhibits peripheral decarboxylation of levodopa, increasing CNS availability and efficacy. Inhaled Levodopa has been developed for rapid relief of off-periods in Parkinson disease because it has fast onset of action and avoid gastrointestinal absorption barriers as an acute dosing form **[26].**Rivastigmine capsules are used in treatment of Alzheimer's disease for Management of cognitive symptoms, Gabapentin, Pregabalin capsules are used to relieve neuropathic pain, and mobility issues. The advantages of oral capsules include Mask unpleasant taste of drugs; better dose flexibility compared to tablets. Limitations of capsules includes Same gastrointestinal limitations as tablets, it is not suitable for individuals with dysphagia, Risk of content spillage if capsules are opened (affecting stability) (Bernsteinian *et al.,* 2023) **[27].**Oral solutions used to assist patients with dysphagia or poor pill tolerance, in such cases Donepezil and Rivastigmine liquid forms improve dosing accuracy and ease of use it is Useful for patients with swallowing problems. But solutions may have stability problems **[28].**

(Levodopa) Inhalation powder is a dry powder formulation which is breathed orally and quickly enters the bloodstream through the lungs. For patients on oral levodopa-dopa decarboxylase inhibitors, it is authorized for on-demand therapy of OFF periods. Two capsules containing 42 mg of levodopa each make up the authorized dose of 84 mg. Five (420 mg) dosages per day is the maximum permitted. By passing across the blood-brain barrier and being transformed into dopamine, levodopa inhalation powder reduces the recurrence of Parkinson's disease symptoms. A breath-actuated inhaler is used to deliver the 84-mg dosage. Parkinson's disease significantly improved with 84 mg. Pharmacokinetics findings indicate that levodopa inhalation powder can be consistently and precisely delivered to the systemic circulation by an inhaled delivery device. Coughing is a common side effect of levodopa inhalation powder, and plasma concentrations of the drug rose more quickly. When Parkinson's disease symptoms resurface, levodopa inhalation powder is meant to be given as an on-demand treatment, with a daily maximum of five doses **[29].**

The oral dosage forms have advantages like enhanced patient compliance, easy self-administration for prolonged treatment, low cost and general availability, suitability for modified-release formulations (including controlled-release levodopa), long shelf life, and comfort. While donepezil can be used in any stage of the illness from mild to moderate to severe rivastigmine and galantamine are mostly used in moderate AD. Inhaled powder including levodopa reaches the systemic circulation through lung delivery **[30].**

Limitations of oral dosage forms include swallowing difficulty in elderly patients, variable bioavailability due to food and gastrointestinal motility disorders, First-pass metabolism reduces drug reaching Central nervous system (CNS). Because of its poor bioavailability and short half-life (6 hours), carvedilol demands a lengthy course of treatment that reduces patient compliance and calls for more frequent dosages. Unsuitable for those with dysphagia, rivastigmine capsules have the same stomach limitations as pills. Oral administration of Rasagiline mesylate can cause bad gastrointestinal adverse effects including headache and vomiting. Oral use of apomorphine calls for large dosages to provide the desired effect, which may include nausea, vomiting, postural hypotension, and renal impairment as shown by elevated urea and creatinine levels **[31].**

3.TRANSDERMAL PATCHES OF CONVENTIONAL DRUGS

BGP-15 (Active ingredient), a yellow substance, is a PARP inhibitor. Typically taken orally, BGP-15 is a capsule. BGP-15 dissolved within the polymer matrix and Transdermal patches were formulated. Among the most often used polymers in transdermal patches to guarantee the appropriate transdermal dosage form for BGP-15 are PVA and PVP **[32].** The different penetration enhancer excipients used in the composition Transductal at 0.1%, Labra sol at 0.1%, or a combination of these two at 0.1% were intended to improve the bioavailability of BGP-15. The mix of Transductal and Labra sol maximized the bioavailability of BGP-15. By helping BGP-15 to reach the systemic circulation, the transdermal patch formulation provides a new therapy approach and improves patient compliance **[33].**

Rivastigmine is a carbamate derivative that acts as a dual inhibitor of acetylcholinesterase (AChe) and butyrylcholinesterase (BuChe), Initially available as oral formulation, Transdermal rivastigmine is used for the treatment of severe AD as well as mild-to-moderate AD **[30].** Early and ongoing treatment using transdermal rivastigmine at

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

a dosage of 13.3 mg/24 h showed clinical improvement in Alzheimer's disease (AD) dementia patients. Usually, the rivastigmine 13.3 mg/24 h patch was well tolerated throughout up to 48-week course of treatment. In 2020, rivastigmine was most often prescribed 9.5 mg/24 hours. An increase to 13.3 mg/24 h may produce some gains for those with mild to moderate AD whose condition worsened while taking the 9.5 mg/24 h patch. Transdermal rivastigmine minimizes fluctuations in plasma levels, lowers maximum plasma concentration, and prolongs the time required to achieve the highest plasma concentration as opposed to oral pills and oral capsules. Moreover, the 9.5 mg/24h patch offers a similar exposure of 12 mg per day of oral medication. Because the transdermal administration approach bypasses the digestive system, it is more tolerable than oral medications. The trial in patients with severe AD showed that the 13.3 mg/24 h patch shows greater efficacy compared with the 4.6 mg/24 h patch with respect to cognition, activities of daily living, and global functioning. Hence evidence supports rivastigmine 13.3 mg/ 24 h transdermal patch as a useful treatment option for patients with mild, moderate, or severe Alzheimer's disease (AD) **[34].**

A beta-adrenergic blocking drug**, Carvedilol** mainly lowers blood pressure, hence leading to beta-adrenoceptor blockade and vasodilation as well as alpha 1-adrenoceptor blockade. Transdermal administration of carvedilol is also possible. Because the transdermal route provides several advantages above oral forms, carvedilol is thought of as a challenging drug possibility for transdermal delivery. Among these characteristics suggesting the ability to pass the lipophilic skin barrier are a high first pass metabolism, a high lipophilicity (log P 3.97), and a low molecular weight (406.5). The matrix-type construction of this formula was selected since it is easy to make and helps to get over the above-mentioned limitation. During the development of Carvedilol transdermal patches, it was found that transdermal patch offers the best option for managing hypertension, it delivers the medicine over a more extended period of time and is also superior to oral administration **[35].**

Amyotrophic lateral sclerosis (ALS) is treated with the benzothiazole molecule and glutamate release inhibitor **Riluzole**, its therapeutic effects arise from its capacity to stop voltage-gated sodium channels, slow down glutamate release, change neurotransmitter signalling, and reduce excitotoxic neuronal damage. Because of its importance, the riluzole transdermal patch which has a low daily dose of 100 mg is a good candidate for TDDS. The ideal patch had a 17% (w/w) riluzole, 10% (w/w) polyglyceryl-3 dioleate (PGD), and a 111-µm adhesive layer **[36].** The ultimate riluzole penetration rate was found to be 2.96 µg. With a log P of 2.3 and a water solubility of 0.0395 mg/mL, riluzole's sustained-release transdermal patch helps to lessen the symptoms. Better stability and increased pharmacokinetic performance are found in the improved formulation. Polyglyceryl-3 dioleate (PGD), a surfactant enhanced drug release and made skin lipids more fluid, therefore improving transdermal absorption, it offers a new approach to treating Amyotrophic lateral sclerosis (ALS) as it can much lower the dosage frequency while still keeping steady plasma levels via controlled medicine delivery **[37].**

Table1 Transdermal patches for Neurodegenerative disorder

S. NO.	DRUG / BIOACTIVE COMPOUND	DISEASE TARGETED	PATCH TYPE / SYSTEM	KEY ADVANTAGES	REFERENCE
1	**Rivastigmine**	Alzheimer's disease	Matrix transdermal patch	Sustained release, reduced GI side effects, improved compliance	[34]
2	**Rotigotine**	Parkinson's disease	Transdermal patch	Continuous dopaminergic stimulation, reduced motor fluctuations	[58]
3	**Riluzole**	ALS	Long-acting transdermal patch	Sustained plasma levels, reduced dosing frequency	[37]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

4	**Rasagiline mesylate**	Parkinson's disease	Microneedle patch	Enhanced bioavailability, painless delivery, controlled release	[25]
5	**Bacopa monnieri (SLNs)**	Parkinson's disease	Microneedle patch	Improved neuroprotection, increased bioavailability, non-irritant	[39]
6	**Betulinic acid**	Neurodegenerative disorders	Polymer-based transdermal patch	Controlled release, enhanced skin permeability, neuroprotection	[40]
7	**Resveratrol (SLNs)**	Parkinson's disease	Microneedle patch	Improved brain delivery, antioxidant effect, sustained release	[42]
8	**Curcumin (SLNs)**	Parkinson's disease	Microneedle patch	Enhanced bioavailability, anti-inflammatory, non-irritant	[45]
9	**Donepezil**	Alzheimer's disease	Microneedle-based transdermal system	Controlled release, improved cognition, reduced GI effects	[54]
10	**Huperzine A**	Alzheimer's disease	Dissolving microneedle patch	Sustained release, improved cognitive outcomes	[47]

4. NATURAL COMPOUNDS FOR NEURODEGENERATIVE DISEASES

Through several neuroprotective mechanisms, plants and fungi are the organic compounds used for their ability to slow the progression of neurodegenerative diseases. Fruits, vegetables, wine, and tea have polyphenols galore**.** Their strong antioxidant and anti-inflammatory characteristics help to reduce neuroinflammation, major contributors to neurodegeneration. Standardizing the dosage and composition of natural substances like resveratrol and curcumin is crucial for steady clinical results. Poor solubility or quick metabolism of many natural molecules restricts their applicability in clinical environments; hence bio availability becomes significant problem **[38].**

In herbal medicine, **Bacopa monnieri**, often known as Brahmi, has been often used to treat a great number of neurological diseases and boost memory and cognitive ability. One soluble microneedle patch loaded with Bacopa. Monnieri claimed as a possible neuroprotective treatment for Parkinson's diseases. The better neuroprotective effect came from the microneedle patch loaded with Bacopa. Monnieri-SLNs than the pure medicine. The improved formulation was tested for skin irritation on rat skin and found not to be sensitizing. Developing Bacopa. Monnieri as a microneedle patch will raise the drug's bioavailability via transdermal absorption and thereby improve its therapeutic effectiveness **[39].**

Betulinic acid, a pentacyclic triterpenoid made by Betula species, offers strong neuroprotective, antioxidant, a possible therapeutic drug for neurodegenerative diseases. Reports indicate that it stops neuroinflammation and lowers oxidative stress, hence protecting neurons against amyloid-β toxicity and mitochondrial dysfunction Its poor water solubility, low oral bioavailability, and great first-pass metabolism restrict its clinical usage **[40].** Improved skin permeability and controlled drug release have been demonstrated with transdermal patches containing betulinic acid manufactured utilizing polymers like ethyl cellulose, PVP, and HPMC. Including penetration enhancers also raises transdermal flow and the efficacy of treatment. Continuous delivery provided by patches helps to keep steady plasma levels, therefore benefiting persistent neurodegenerative disorders **[41].**

Resveratrol Found in red wine and grapes, it reduces oxidative stress and controls inflammatory processes, hence acting neuroprotective. Naturally occurring polyphenolic molecule resveratrol shows neuroprotective, antioxidant, and anti-inflammatory properties, hence it is a possible treatment for neurodegenerative diseases **[42].** low oral bioavailability, poor water solubility, fast metabolism, and inadequate brain distribution limit its clinical use, therefore stimulating research into new delivery systems,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

these include resveratrol-loaded solid lipid nanoparticles included in microneedle patches. Preclinical studies showed that these transdermal microneedle patches provided better skin penetration, extended-release profiles, and greater plasma and brain bioavailability, therefore conquering traditional administration problems and improving therapeutic effects in Parkinson's disease models. These modern patches shown remarkable increases in brain antioxidant levels and behavioural performance with hardly any skin irritation, therefore highlighting their potential in the treatment of persistent neurodegenerative disorders. Percutaneous absorption and medication retention are enhanced by combining resveratrol into nano-enabled patch matrices, therefore addressing solubility and stability issues. Understanding the whole therapeutic potential of resveratrol in neurodegeneration depends on continuous patch composition refinement, permeability enhancement, and clinical validation **[43].**

Curcumin is a prospective therapy for neurodegenerative disorders. Its poor water solubility, bioavailability, rapid metabolism, and restricted penetration across the blood-brain barrier limit its clinical use **[44].** To overcome these obstacles, new delivery techniques including curcumin-loaded solid lipid nanoparticles inserted into transdermal patches and microneedle have been developed**.** With enhanced motor coordination, balance, and a reduced degree of bradykinesia, the made microneedles were also shown to be non-irritant. Using a new microneedle loaded with curcumin-loaded solid lipid nanoparticles as a possible treatment for Parkinson's disease was theoretically justified in the study **[45].**

Green tea - Camellia sinensis (L.) Kuntze., has polyphenol, epigallocatechin gallate, which protects neurons due to its property of reducing inflammation and scavenging free radicals. Polyphenol epigallocatechin gallate of green tea has also been explored in patients and Huntington's disease (HD) models. It had proved to possess the capability of improving cognitive and motor skills. As oxidative stress and excitotoxicity form the characteristics of HD, the antioxidant property of EGCG played a major role in mitigating the conditions **[46].**

Plants and microbes produce alkaloids; They are renowned for their power to regulate neurochemicals and raise cognitive capacity. An acetylcholinesterase inhibitor generated from the (Hesperia serrata (Thunb.) Trevis, Fam: Lycopodiaceae), **Huperzine A** is a substance that boosts acetylcholine levels and improves cognitive performance and memory in people with Alzheimer's disease. By regulating glucose metabolism, berberine an alkaloid found in Berberi's species shows anti-inflammatory properties and may be used in both models of Alzheimer's disease (AD) and Parkinson's disease (PD) **[47].**

Terpenoids are common in essential oils and contribute to the aroma of plants. They possess antioxidant and anti-inflammatory properties beneficial for the protection of neuronal health. **Ginkgolides**, found in the Ginkgo biloba L. (Ginkgoaceae family), possess antioxidant action and promote blood flow. They protect the brain against conditions like dementia. Various clinical studies on the use of ginkgo biloba extracts have been observed, particularly in Asian countries and Europe. The proposed mechanism of the neuroprotective action of Ginkgo biloba extract lies in its antioxidant property and inability to increase blood flow to the brain, protecting the neuronal tissue against the oxidative stress **[48].**

Cannabidiol (CBD) extracted from the plant Cannabis sativa (Cannabaceae family), also holds promise in the enhancement of neurogenesis and reducing neuro-inflammation. Omega-3 fatty acids found in fish oil work well in enhancing the lipid fluidity of neuronal membranes and exhibit anti-inflammatory properties and could be useful in the treatment and control of AD and PD **[49]. Astaxanthin** is a carotenoid antioxidant found in shellfish, shrimp, trout, salmon seafood, and in certain microalgae. Astaxanthin contains a ketone and hydroxyl moiety. Activation of the antioxidant response element protects cells against oxidative insult and inflammation. Being the activators of the antioxidant defender catalase and the super oxide dismutase enzyme (SOD), which protects the cell against oxidative insult and inflammation, it is classified as an antioxidant with strong neuroprotective properties. Astaxanthin demonstrates strong anti-inflammatory properties within the nervous system. The mechanism involves the potent inhibition of the inflammatory process and the protection of neurons within AD and PD. **[50].**

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

5. ADVANCED TECHNIQUES FOR TRANSDERMAL DRUG DELIVERY

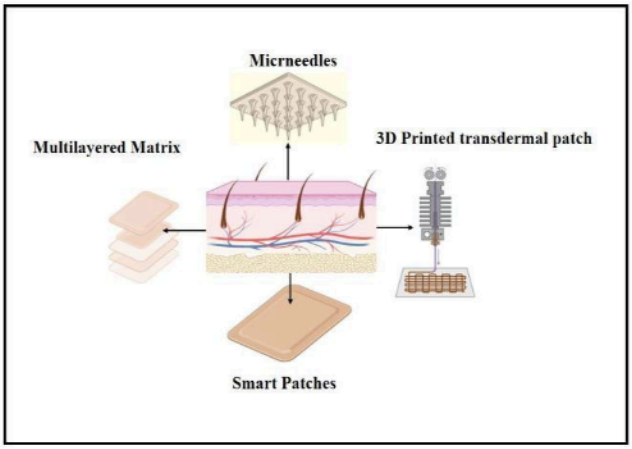


Fig2: Advanced transdermal systems

5.1MICRONEEDLE PATCHES IN NEURO-DEGENERATIVE DISEASE

Microneedle patches are an innovative, low-invasive transdermal drug distribution method with much promise for treating neurodegenerative diseases **[51].** By avoiding first-pass metabolism, improving bioavailability, and boosting patient compliance as well as by overcoming the drawbacks of oral/parenteral administration; Recent research focus on their use of many neurotherapeutic medications. **[52].** Microneedles developed using monoamine oxidase-B (MAO-B) inhibitor rasagiline mesylate hydrogels showed noteworthy results for Parkinson's diseases. For long-lasting transdermal delivery, these microneedles show great mechanical strength, regulated medicine release, and notable skin penetration. To reduce oxidative stress in models of neurological illnesses, new microneedle patches loaded with the hydrogen sulphide donor AP39 have been developed. In lowering neurodegeneration loads following transdermal administration, they have shown great promise **[53].** Better cognitive outcomes, sustained release, and longer half-life have been observed in preclinical Alzheimer's disease models employing dissolving microneedles to administer huperzine A trans dermally, hence showing their ability to enhance the therapeutic indices of medications with low oral bioavailability **[54].** Hybrid systems of donepezil-loaded microparticle depots loaded dissolved micro needle patches designed for long intradermal delivery targeted for Alzheimer's treatment demonstrated more consistent release profiles than do traditional patches **[55].**

Other studies include polymeric microneedles for the administration of rivastigmine, a medication used to treat dementia, which demonstrate improved regulated release and effective skin penetration for perhaps anti-dementia medication;**[56].** Recent assessments of microneedle methods emphasize their biocompatibility, biodegradability, ability to create microchannels facilitating systemic medication delivery, and ability to alleviate suffering and gastrointestinal barriers**;[57]**. The rising clinical interest in Parkinson's, Alzheimer's, and other neurodegenerative diseases suggests that microneedle-mediated drug delivery systems offer painless, sustained, and effective ways of neurologic medication administration. Among current issues are those of maximizing the drug loading capacity, improving sustained release characteristics, improving blood-brain barrier penetration where required, and validating the long-term safety and efficacy in vivo **[58]** Future studies should concentrate on merging stimuli-responsive and multifunctional microneedle designs that permit regulated/on-demand medicine release so as to maximize therapeutic benefits for neurodegenerative diseases and speed up the clinical application of these promising transdermal technologies using polymers and nanotechnology **[59].**

5.2 ROLE OF 3D PRINTING FOR NEURO-DEGENERATIVE DISEASES

3D printing techniques may produce three-dimensional items with complex geometries and details, choosing a 3D printing technology greatly improves the complexity, accuracy, and material compatibility of implantable microelectrodes **[60].**3D-printed microneedles provide a workable alternative to solve these problems. With the right dimensions, forms, and materials, researchers can produce minimally invasive equipment that can pierce the mucosal barriers or outer layers of the skin **[61].** To enable therapeutic drugs to penetrate the BBB (blood brain barrier) or to provide medicines directly into the tissues around the brain, these microneedles can be modified Furthermore, 3D printing microneedles enables to be customized to improve drug release profiles and boost targeting accuracy, therefore maybe increasing the efficacy of drug distribution to the brain and lowering negative effects connected with systemic administration **[62].**

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

There are several benefits to 3D printing, including quick prototyping, scalability, design versatility, and customization which are represented in the Table 2. Researchers may create microelectrodes with specific geometries and characteristics using 3D printing, and they can also tailor their performance for particular uses. The chosen approach will influence the device's performance, biocompatibility, complexity, and precision **[63].**

5.3 FROM BIOMARKERS TO PRECISION MEDICINE IN NEURODEGENRATIVE DISEASES

For neurodegenerative diseases, the preferred method has become precision medicine, which goes beyond single biomarker usage and toward an integrated, patient-centered approach leveraging molecular, genetic, clinical, and imaging data to help diagnose, predict, and treat **[64].** Although biomarkers continue to be essential for early detection, disease staging, and course monitoring, they are most effective when integrated into a more extensive accuracy paradigm considering individual differences in disease mechanisms, risk profiles, and treatment reaction **[65].** Given the diversity of neurodegenerative diseases, even within the same diagnostic group one-size-fits-all cures are inadequate for proper management. By integrating genomics, proteomics, metabolomics, digital phenotyping with indicators including amyloid-β, tau, α-synuclein, neurofilament light chain, and markers of neuroinflammation, precision medicine generates different disease trajectories **[66].** This method enables informed therapeutic choices, improves prognostic stratification, and helps to generate earlier and more precise diagnoses. Importantly, precision medicine helps us to find those who have presymptomatic symptoms and are at risk, hence enabling us to quickly act before lasting brain damage develops. Better patient selection, outcome prediction, and response monitoring are made possible by it, therefore improving clinical trial design by enhancing the probability of therapeutic success **[67].** Ultimately, precision medicine offers the best chance to create treatments that change the course of neurodegenerative disorders, improve patient care, and lower the worldwide burden of such diseases than do biomarker-only strategies **[68]**

Table 2 3D printing Technology

S.NO	TECHNIQUE	PROCESS	MATERIAL	ADVANTAGE	DISADVANTAGES	REF
1	**STEREOLITHOGRAPHY (SLS)**	liquid resin is hardened layer by layer by using a Laser.	resins, plastics, ceramics, and metals	high resolution	limited material choices require postprocessing	[51]
2	**SELECTIVE LASER SINTERING(SLS)**	Powdered material is fused layer by layer using a laser.	metals, ceramics, polymers	wide range of materials, good mechanical properties	limited resolution requires postprocessing	[52]
3	**FUSED DISPOSITION MODELLING(FDM)**	The thermoplastic filament is extruded layer by layer from a melting nozzle.	thermoplastics, hydrogels	low cost, high speed	limited resolution, poor surface finish	[61]
4	**DIGITAL LIGHT PROCESSING(DLP)**	UV light is projected by a light projector	photopolymers	good surface finish, high resolution,	postprocessing required due to limited material choices	[62]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

		onto a tank of photo-sensitive resin, causing it to solidify layer by layer.				
5	**TWO-PHOTON POLYMERIZATION(2PP)**	A photo-sensitive resin is polymerized by a laser, resulting in complex architectures.	photopolymers and hydrogels.	Ability to create complex structures.	limited build volume, slow speed, expensive	[63]

5.4 ROLE OF PERSONALIZED MEDICINE IN NEURODEGENRATIVE DISEASES

Personalized medicine for neurodegenerative diseases guarantees a paradigm change in both knowledge and management of diseases; Using tailored techniques combining genetic, epigenetic, molecular, imaging, and clinical data to stratify patients for customized therapies; **[69].**emerging biomarkers allow earlier and more precise diagnosis and risk assessment beyond one-size-fits-all treatments; Progress in pharmacoepigenomics and epigenetics is identifying patient-specific modifications that may direct customized pharmacotherapy and increase effectiveness while minimizing adverse effects by combining sequencing and genetic approaches **[70].** Programs in pharmacogenomics utilizing indicators like APOE,

CYP2D6, and others demonstrate the potential of enhancing medicine choice and dosage depending on genetic profile **[71].** Stratification and prognosticating are anticipated from research of multimodal biomarkers that is, fluid and neuroimaging signatures using machine learning. Targeted molecular and cellular disease pathways help to develop precise therapies meant to maximize efficacy and minimize off-target effects. Future looks bright for combination therapies, which simultaneously attack several pathways **[72].** Despite major obstacles, including translating basic results into clinically effective medicines, negotiating the blood-brain barrier, guaranteeing long-term safety, and reaching affordable implementation, there are still some challenges **[73].** Data privacy, legal, and ethical frameworks must develop in order to ensure safety access. Customized methods validated from large, diverse datasets will be developed via collaborative networks among medical professionals, scientists, and business. **[74].** Dynamic therapy approaches that change with time will better mirror each patient's unique disease trajectory than will statically models **[75].** Finally, a very customized medicine approach that might change the course of neurodegenerative illnesses and improve clinical results will come about through the integration of biomarkers, genomics, cell models, precision treatments, and artificial intelligence **[76].**

6. CONCLUSION

For the therapy of neurodegenerative disorders, transdermal patches seem to be the most suitable for future approach. Low bioavailability, first-pass metabolism, and poor patient compliance restrict the long-term efficacy of standard oral medications. By avoiding hepatic metabolism, alternative transdermal systems provide controlled and continuous drug administration. Though 3D-printed based transdermal patches are now limited and not developed, this technique has great possibilities for tailored medicine. With 3D printing, drug dosage, release rate, and design of patch can be selected according to the needs of each patient. Reduced dosing frequency may be achieved by extended drug release, which might span weeks, months, or even a year. Eliminating the need for daily tablet use could help to increase patient compliance and adherence to medication. Furthermore, customized controlled-release patches might improve patient comfort and clinical outcomes. Bioactive compound–based transdermal patches are still underexplored for neurodegenerative diseases, highlighting a major research opportunity. Advances in 3D printing of bioactive

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

compound loaded hydrogels might enable precise dose control, improved bioavailability, and extended drug release from such patches eliminating adverse effects. These technologies overcome limitations of conventional delivery, enhance therapeutic efficacy and will be future approach for treating neurodegenerative diseases.

DECLARATION

The authors discloses no conflict of interest.

REFERENCES:

1. Dugger BN, Dickson DW. Pathology of neurodegenerative diseases. Cold Spring Harbor perspectives in biology. 2017 Jul 1;9(7):a028035.
2. He J, Zhang Y, Yu X, Xu C. Wearable patches for transdermal drug delivery. Acta pharmaceutica sinica B. 2023 Jun 1;13(6):2298-309.
3. Singh S, Rajput DS, Gupta N, Sharma B, Rathi S, Singh A. A Brief Review on Transdermal Patches. Chinese Journal of Applied Physiology. 2025 Jun 23:e20250013.
4. Gaikwad SS, Zanje AL, Somwanshi JD. Advancements in transdermal drug delivery: A comprehensive review of physical penetration enhancement techniques. International Journal of Pharmaceutics. 2024 Mar 5;652:123856.
5. Liu E, Zhang Y, Wang JZ. Updates in Alzheimer's disease: from basic research to diagnosis and therapies. Translational Neurodegeneration. 2024 Sep 4;13(1):45.
6. Bloem BR, Okun MS, Klein C. Parkinson's disease. The Lancet. 2021 Jun 12;397(10291):2284-303.
7. Sales de Campos P, Olsen WL, Wymer JP, Smith BK. Respiratory therapies for Amyotrophic Lateral Sclerosis: A state of the art review. Chronic respiratory disease. 2023 May 9;20:14799731231175915.
8. Olmedo-Saura G, Bernardi E, Bojtos L, Martínez-Horta S, Pagonabarraga J, Kulisevsky J, Pérez-Pérez J. Update on the symptomatic treatment of Huntington's disease: from pathophysiology to clinical practice. International journal of molecular sciences. 2025 Jun 27;26(13):6220.
9. Singh B, Day CM, Abdella S, Garg S. Alzheimer's disease current therapies, novel drug delivery systems and future directions for better disease management. Journal of Controlled Release. 2024 Mar 1;367:402-24.
10. Chopade P, Chopade N, Zhao Z, Mitragotri S, Liao R, Chandran Suja V. Alzheimer's and Parkinson's disease therapies in the clinic. Bioengineering & Translational Medicine. 2023 Jan;8(1):e10367.
11. Saha P, Roy SJ, Bhattacharya S, Datta A. Intranasal delivery of therapeutics to degenerating brain regions: From pathways to nanocarriers. Journal of Drug Delivery Science and Technology. 2025 Nov 22:107818.
12. Wang Y, Wu S, Chen J, Yang S, Wu C, Zhao Q, Zhang H, Wei K, Zhang J, Zhang R, Yang L. Transdermal drugs and delivery strategies: History, advances and future prospects. Chinese Chemical Letters. 2025 Nov 25:112170.
13. García Ribas G, Ferrer-Picón E. Tolerability of rivastigmine transdermal patch in patients with Alzheimer's disease: a narrative review. Expert Opinion on Drug Safety. 2025 Nov 2:1-3.
14. Gattu K, Godugu D, Jain H, Jadhav K, Cho H, Rojekar S. Microneedle Technologies for Drug Delivery: Innovations, Applications, and Commercial Challenges. Micromachines. 2026 Jan 13;17(1):102.
15. Balakrishnan P, Junaid S, Ahmad S, Wang K, Hindalekar YS, Shokr H, Upadhya M, Hopkins S, Sacharczuk J, Singh Rana K, Anas Al Tahan M. Novel microneedle patches for transdermal delivery of AP39, a hydrogen sulphide donor, in the treatment of scenarios mimicking neurological disorders. Journal of Pharmaceutical Investigation. 2025 Jul;55(4):603-16.
16. Madhusoodanan G, Roy AA, Kalkundri T, Preman NK, Rana K, Datta D, Dhas N, Mutalik S. Evolving transdermal therapeutics: a review on self-dissolving polymeric microneedles via 3D printing. RSC advances. 2025;15(40):33312-35.
17. Michael B, Jayaprakash N, Munivel N, Jaisankar D. 3D printing in drug delivery: emerging technologies, clinical translation, and the future of personalized medicine. Medicine in Drug Discovery. 2025 Dec 13:100242.
18. Prajapat M, Gholap AD, Shinde S, Padhiyar D, Butani S, Shah S, Rajput A. 3D printing technology in microneedles: An emerging era in transdermal drug delivery. Hybrid Advances. 2025 Sep 1;10:100447.
19. Karve T, Dandekar A, Agrahari V, Peet MM, Banga AK, Doncel GF. Long-acting transdermal drug delivery formulations: Current developments and innovative pharmaceutical approaches. Advanced drug delivery reviews. 2024 Jul 1;210:115326.
20. Goyal R, Mittal P, Gautam RK, Kamal MA, Perveen A, Garg V, Alexiou A, Saboor M, Haque S, Farhana A, Papadakis M. Natural products in the management of neurodegenerative diseases. Nutrition & metabolism. 2024 May 16;21(1):26.
21. Sequeira L, Benfeito S, Fernandes C, Lima I, Peixoto J, Alves C, Machado CS, Gaspar A, Borges F, Chavarria

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

D. Drug development for Alzheimer's and Parkinson's disease: where do we go now?. Pharmaceutics. 2024 May 24;16(6):708.

22. Palanisamy CP, Pei J, Alugoju P, Anthikapalli NV, Jayaraman S, Veeraraghavan VP, Gopathy S, Roy JR, Janaki CS, Thalamati D, Mironescu M. New strategies of neurodegenerative disease treatment with extracellular vesicles (EVs) derived from mesenchymal stem cells (MSCs). Theranostics. 2023 Jul 16;13(12):4138.
23. Thawabteh AM, Ghanem AW, AbuMadi S, Thaher D, Jaghama W, Karaman D, Karaman R. Recent advances in therapeutics for the treatment of Alzheimer's disease. Molecules. 2024 Oct 30;29(21):5131.
24. Attia MS, Hasan AA, Ghazy FE, Gomaa E. Mesoporous silica nanoparticles-embedded hydrogel: A potential approach for transdermal delivery of carvedilol to pediatric population. International Journal of Pharmaceutics. 2025 May 15;676:125605.
25. Yalcin TE, Anjani QK, Li Y, Larrañeta E, Paredes AJ, Donnelly RF. Rasagiline mesylate-based microneedle patches: A patient-friendly treatment regimen for Parkinson's disease. International Journal of Pharmaceutics. 2025 Jul 30:126019.
26. Muranova A, Shanina E. Levodopa/carbidopa/entacapone combination therapy. InStatPearls [Internet] 2023 Dec 7. StatPearls Publishing.
27. Amanatkar HR, Grossberg GT. Transdermal rivastigmine in the treatment of Alzheimer's disease: current and future directions. Expert Review of Neurotherapeutics. 2014 Oct 1;14(10):1119-25.
28. Frota BM, Holanda SN, Sousa FB, Alves AP. Evaluation of oral conditions in patients with neurodegenerative diseases treated in geriatric centers. RGO-Revista Gaúcha de Odontologia. 2016;64:17-23.
29. Hauser RA, LeWitt PA, Waters CH, Grosset DG, Blank B. The clinical development of levodopa inhalation powder. Clinical neuropharmacology. 2023 Mar 1;46(2):66-78.
30. Gadhave DG, Sugandhi VV, Jha SK, Nangare SN, Gupta G, Singh SK, Dua K, Cho H, Hansbro PM, Paudel KR. Neurodegenerative disorders: Mechanisms of degeneration and therapeutic approaches with their clinical relevance. Ageing research reviews. 2024 Aug 1;99:102357.
31. Mathur S, Gawas C, Ahmad IZ, Wani M, Tabassum H. Neurodegenerative disorders: assessing the impact of natural vs drug-induced treatment options. Aging Medicine. 2023 Mar;6(1):82-97.
32. Pető Á, Kósa D, Haimhoffer Á, Fehér P, Ujhelyi Z, Sinka D, Fenyvesi F, Váradi J, Vecsernyés M, Gyöngyösi A, Lekli I. Nicotinic amidoxime derivate bgp-15, topical dosage formulation and anti-inflammatory effect. Pharmaceutics. 2021 Nov 29;13(12):2037.
33. Bácskay I, Hosszú Z, Budai I, Ujhelyi Z, Fehér P, Kósa D, Haimhoffer Á, Pető Á. Formulation and evaluation of transdermal patches containing BGP-15. Pharmaceutics. 2023 Dec 27;16(1):36.
34. Fortea J, Ferrer-Picón E. An overview of the rivastigmine 13.3 mg/24h transdermal patch as a treatment option for Alzheimer's disease. Expert Review of Neurotherapeutics. 2025 Sep 2(just-accepted).
35. Mo L, Lu G, Ou X, Ouyang D. Formulation and development of novel control release transdermal patches of carvedilol to improve bioavailability for the treatment of heart failure. Saudi journal of biological sciences. 2022 Jan 1;29(1):266-72.
36. Ashfaq A, Riaz T, Waqar MA, Zaman M, Majeed I. A comprehensive review on transdermal patches as an efficient approach for the delivery of drug. Polymer-Plastics Technology and Materials. 2024 May 23;63(8):1045-69.
37. Liu Y, Chen G, Li M, Li M, Xie D, Luo Z. Development of long-acting riluzole transdermal patch against amyotrophic lateral sclerosis: Mechanistic insights into polyglyceryl-3 dioleate-enhanced drug release and skin permeation. International Journal of Pharmaceutics: X. 2025 Jul 20:100363.
38. Guan Y, Li L, Yang R, Lu Y, Tang J. Targeting mitochondria with natural polyphenols for treating Neurodegenerative Diseases: a comprehensive scoping review from oxidative stress perspective. Journal of Translational Medicine. 2025 May 23;23(1):572.
39. Joy D, Jose J, Bibi S, Bandiwadekar A, Gopan G, Mariana Gonçalves Lima C, Bin Emran T, A. Alhumaydhi F, Ashtekar H, D. S S, Adam Conte-Junior C. [Retracted] Development of Microneedle Patch Loaded with Bacopa monnieri Solid Lipid Nanoparticles for the Effective Management of Parkinson's Disease. Bioinorganic Chemistry and Applications. 2022;2022(1):9150205.
40. Kumar M, Bose P, Singh AP, Singh AP. Formulation and Evaluation of Betulinic Acid Loaded Transdermal Patches. Journal of Drug Delivery & Therapeutics. 2025 Jan 1;15(1).
41. Tsai CW, Tsai RT, Liu SP, Chen CS, Tsai MC, Chien SH, Hung HS, Lin SZ, Shyu WC, Fu RH. Neuroprotective effects of betulin in pharmacological and transgenic Caenorhabditis elegans models of Parkinson's disease. Cell transplantation. 2017 Dec;26(12):1903-18.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

42. Bandiwadekar A, Jose J, Khayatkashani M, Habtemariam S, Khayat Kashani HR, Nabavi SM. Emerging novel approaches for the enhanced delivery of natural products for the management of neurodegenerative diseases. Journal of Molecular Neuroscience. 2022 Mar;72(3):653-76.
43. Bandiwadekar A, Jose J, Gopan G, Augustin V, Ashtekar H, Khot KB. Transdermal delivery of resveratrol loaded solid lipid nanoparticle as a microneedle patch: a novel approach for the treatment of Parkinson's disease. Drug delivery and translational research. 2025 Mar;15(3):1043-73.
44. Kalambhe DR, Shelke OS, Deshpande AH, Huang Y. In-vitro Efficacy and In-vivo Safety Study of a Transdermal Formulation Containing Flavonoid-Rich Extract from Curcuma Longa L. Journal of Pharmaceutical Innovation. 2026 Feb;21(1):44.
45. Esmaealzadeh N, Miri MS, Mavaddat H, Peyrovinasab A, Ghasemi Zargar S, Sirous Kabiri S, Razavi SM, Abdolghaffari AH. The regulating effect of curcumin on NF-κB pathway in neurodegenerative diseases: a review of the underlying mechanisms. Inflammopharmacology. 2024 Aug;32(4):2125-51.
46. Fernandes L, Cardim-Pires TR, Foguel D, Palhano FL. Green tea polyphenol epigallocatechin-gallate in amyloid aggregation and neurodegenerative diseases. Frontiers in neuroscience. 2021 Sep 14;15:718188.
47. Dadgostar E, Moghanlou M, Parvaresh M, Mohammadi S, Khandan M, Aschner M, Mirzaei H, Tamtaji OR. Can berberine serve as a new therapy for Parkinson's disease?. Neurotoxicity Research. 2022 Aug;40(4):1096-102
48. Eckert A, Georgescu D, Seifritz E, Müller WE. Improvement of age-related neurocognitive disorders by Ginkgo biloba extract: neuroprotection in focus. International Journal of Psychiatry in Clinical Practice. 2026 Jan 23:1-4.
49. Zhang Z, Yin L, Yang Q, Guo F, Wang X, Chen F, Yang G. Dissolving microneedles for transdermal delivery of huperzine A for the treatment of Alzheimer's disease. Drug Delivery. 2020 Jan 1;27(1):1147-55.
50. Tanveer R, McGuinness N, Daniel S, Gowran A, Campbell VA. Cannabinoid receptors and neurodegenerative diseases. Wiley Interdisciplinary Reviews: Membrane Transport and Signaling. 2012 Sep;1(5):633-9.
51. Razzaghi M. Polymeric 3D-printed microneedle arrays for non-transdermal drug delivery and diagnostics. Polymers. 2025 Jul 18;17(14):1982.
52. Mahamuni SS, Desai MM, Thorawades KM, Bhagwat DA. Advances in 3D-printed transdermal microneedle patches for antifungal therapy: Current scenario and challenges. Current Opinion in Pharmacology. 2025 Aug 1;83:102545.
53. Anjani QK, Moreno-Castellanos N, Li Y, Sabri AH, Donnelly RF. Dissolvable microarray patches of levodopa and carbidopa for Parkinson's disease management. European Journal of Pharmaceutics and Biopharmaceutics. 2024 Jun 1;199:114304.
54. Yan Q, Wang W, Weng J, Zhang Z, Yin L, Yang Q, Guo F, Wang X, Chen F, Yang G. Dissolving microneedles for transdermal delivery of huperzine A for the treatment of Alzheimer's disease. Drug Delivery. 2020 Jan 1;27(1):1147-55.
55. Lee JH, Song GJ, Hwang HS, Lee CS. Dissolving microneedle patch integrated with microparticle depots for sustained intradermal delivery of donepezil. International Journal of Pharmaceutics. 2025 Jun 10;678:125653.
56. Monou PK, Andriotis E, Tzetzis D, Tzimtzimis E, Panteris E, Andreadis D, Demiri E, Vizirianakis IS, Fatouros DG. Evaluation of 3D-printed solid microneedles coated with electrosprayed polymeric nanoparticles for simultaneous delivery of rivastigmine and N-acetyl cysteine. ACS Applied Bio Materials. 2024 Apr 9;7(5):2710-24.
57. Nguyen HX, Banga AK. Advanced transdermal drug delivery system: A comprehensive review of microneedle technologies, novel designs, diverse applications, and critical challenges. International Journal of Pharmaceutics. 2025 Feb 10;670:125118.
58. Mahdiyyah A, Diyah N, Hendradi E. Transdermal Patches: A review of a new drug delivery system approach. International Journal of Medical Reviews and Case Reports. 2022 Aug 21;6(9):25-.
59. Li J, Xia Q, Ma S, Wang Z, Guo T, Feng N, Zhang Y. Progressive microneedles for targeting and intelligent drug delivery. Asian Journal of Pharmaceutical Sciences. 2025 Jun 1;20(3):101051.
60. Yuvaraj AR, Jayadurka J, Elavarasi E, Srinivasan R. Applications and Advancement of 3D Printing in Pharmaceutical Manufacturing and Drug Delivery. Journal of Pharma Insights and Research. 2024 Jun 1;2(3):023-9.
61. Gander C, Shi K, Nokhodchi A, Lam M. A review of the benefits 3D printing brings to patients with neurological diseases. Pharmaceutics. 2023 Mar;15(3):892.
62. Whitehouse C, Corbett N, Brownlees J. 3D models of neurodegeneration: implementation in drug discovery. Trends in Pharmacological Sciences. 2023 Apr 1;44(4):208-21.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(3), 3911-3924 | ISSN:2251-6727

63. Wojtyłko M, Lamprou DA, Froelich A, Kuczko W, Wichniarek R, Osmałek T. 3D-printed solid oral dosage forms for mental and neurological disorders: Recent advances and future perspectives. Expert Opinion on Drug Delivery. 2024 Nov 1;21(11):1523-41.
64. Tondo G, De Marchi F. From biomarkers to precision medicine in neurodegenerative diseases: Where are we?. Journal of Clinical Medicine. 2022 Aug 3;11(15):4515
65. Strianese O, Rizzo F, Ciccarelli M, Galasso G, D'Agostino Y, Salvati A, Del Giudice C, Tesorio P, Rusciano MR. Precision and personalized medicine: how genomic approach improves the management of cardiovascular and neurodegenerative disease. Genes. 2020 Jul 6;11(7):747
66. Gunasekaran B, Arifin AH, Yu WH, Hanafi S, Rao KD, Salvamani S. Precision medicine in neurodegenerative diseases: From research to clinical practice. Progress in Brain Research. 2025 Nov 14;297:1-52.
67. Cummings JL, Teunissen CE, Fiske BK, Le Ber I, Wildsmith KR, Schöll M, Dunn B, Scheltens P. Biomarker-guided decision making in clinical drug development for neurodegenerative disorders. Nature Reviews Drug Discovery. 2025 Aug;24(8):589-609.
68. Braudeau J, Souchet B, Streel E. Optimizing Alzheimer's diagnosis and precision medicine: A narrative review unlocking the potential of multiomics markers. NeuroMarkers. 2025 Sep 1;2(3):100107.
69. Pandey S, Jirásko M, Lochman J, Chvátal A, Chottova Dvorakova M, Kučera R. iPSCs in neurodegenerative disorders: A unique platform for clinical research and personalized medicine. Journal of Personalized Medicine. 2022 Sep 10;12(9):1485.
70. Dong JM, Zhong H. Systematic Review: Proteomics-Driven Multi-Omics Integration for Alzheimer's Disease Pathology and Precision Medicine. Neurology International. 2025 Dec 2;17(12):197.
71. Ahmad SR, Zeyaullah M, Khan MS, AlShahrani AM, Altijani AA, Ali H, Dawria A, Mohieldin A, Alam MS, Mohamed AO. Pharmacogenomics for neurodegenerative disorders-a focused review. Frontiers in Pharmacology. 2024 Dec 20;15:1478964.
72. Wahul RM, Ambadekar S, Dhanvijay DM, Dhanvijay MM, Dudhedia MA, Gaikwad V, Kanawade B, Pansare JR, Bodkhe B, Gawande SH. Multimodal approaches and AI-driven innovations in dementia diagnosis: a systematic review. Discover Artificial Intelligence. 2025 Jun 10;5(1):96.
73. Yang HM. Overcoming the Blood–Brain Barrier: Advanced Strategies in Targeted Drug Delivery for Neurodegenerative Diseases. Pharmaceutics. 2025 Aug 11;17(8):1041.
74. Elhussein A, Baymuradov U, Elhadad N, Natarajan K, Gürsoy G. A framework for sharing of clinical and genetic data for precision medicine applications. Nature medicine. 2024 Dec;30(12):3578-89.
75. Banumathi K, Venkatesan L, Benjamin LS, Vijayalakshmi K, Satchi NS, Satchi IV NS. Reinforcement learning in personalized medicine: a comprehensive review of treatment optimization strategies. Cureus. 2025 Apr 21;17(4).
76. Alshehri ZS. Integrating artificial intelligence with small molecule therapeutics and precision medicine for neurochemical understanding of Alzheimer's diseases. Neuroscience. 2025 Sep 18.