IJPSR (2026), Volume 17, Issue 1 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 02 July 2025; received in revised form, 15 July 2025; accepted, 21 July 2025; published 01 January 2026

NANOMEDICINE FOR HUNTINGTON'S DISEASE: A REVIEW OF CURRENT STRATEGIES, CHALLENGES, AND FUTURE DIRECTIONS

M. V. Neethu [*1], Shubham Sharma [2], Neha Narwal [2], Sapna Kumari [2] and V. M. Anjumol [3]

Mets College of Pharmaceutical Sciences & Research [1], Kuruvilassery P.O, Mala, Thrissur - 680732, Kerala, India.
Amity Institute of Pharmacy [2], Amity University Madhya Pradesh, Gwalior, near Maharjpura, Gwalior - 474005, Madhya Pradesh, India,
Department of Pharmaceutical Sciences [3], Cheruvandoor - 686637, Kerala, India.

Keywords:

Huntington's disease, Neurodegenerative disorder, Drug delivery, Barrier, Nanotechnology, Neuroprotection

Correspondence to Author:
M. V. Neethu

Assistant Professor,
Mets College of Pharmaceutical Sciences & Research, Kuruvilassery P.O, Mala, Thrissur - 680732, Kerala, India.

E-mail: pr.mvneethu@gmail.com

ABSTRACT: Mutations in the HTT gene cause Huntington's disease (HD), a hereditary neurological disorder. These mutations lead to the accumulation of the mutant huntingtin protein, which results in neuronal dysfunction and progressively worsening mental, cognitive, and physical symptoms. In Western populations, the prevalence of HD ranges from 10.6 to 13.7 cases per 100,000. Huntington's disease does not yet have a cure; the main treatments for its symptoms are cognitive and psychiatric issues, chorea, psychosis, and dystonia. Among the therapeutic issues that need to be addressed are poor drug distribution across the blood-brain barrier (BBB) and off-target effects caused by the BBB's restricted permeability. Nanotechnology provides novel methods and insights that can improve therapy effectiveness, neuroprotection, and customized drug delivery. This review article discusses Huntington's disease's aetiology, epidemiology, pathophysiology, symptoms, current treatments, nanotherapy, and ongoing clinical studies. Despite numerous challenges, this review highlights the advancements in nanotechnology for HD therapy, the possibility of overcoming present barriers, improving patient outcomes, and the need for additional research to fully understand long-term health effects.

INTRODUCTION: In contrast to the focused neuronal damage brought on by metabolic or chemical insults, neurodegenerative illnesses are characterized by the gradual degeneration of particular groups of susceptible neurons. The presence of proteins with aberrant conformations is a crucial feature of these diseases [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.17(1).75-90

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.17(1).75-90

Neurodegenerative diseases pose a serious threat to future generations and are a major worldwide health problem because of their genetic inheritance patterns. These neurodegenerative disorders include amyotrophic lateral sclerosis (ALS), Alzheimer's disease (AD), Parkinson's disease (PD), and Huntington's disease (HD) [2].

Huntington's disease is caused by a mutation in the HTT gene and is inherited autosomally dominantly. Patients and their families are profoundly impacted by this serious neurological condition. It usually first appears in early or mid-adulthood and gets worse with time. A variety of symptoms, such as behavioural abnormalities, cognitive decline, and

motor dysfunction, are indicative of HD. An enlarged CAG trinucleotide sequence in the huntingtin protein-encoding HTT gene is the primary cause. This expansion causes the protein's polyglutamine tracts to become abnormally lengthy in afflicted individuals. These structural changes weaken the stability of proteins and increase their propensity to misfold and break down, which ultimately results in neuronal death and functional degradation [2-4].

Nanotechnology is enabling a breakthrough in the treatment of neurodegenerative illnesses. Small size, increased surface area, improved BBB penetration, and well-defined particle size and shape are characteristics that set nanoparticles apart. Immunomodulation, autophagy induction, Huntington gene (HTT) suppression, HTT protein modification or inactivation, and N-methyl-d-aspartate (NMDA) extra synaptic receptor inhibition are among the nanoparticle-based treatments for HD [5]. Nanotherapeutics have the potential to treat HD because of their capacity to precisely target and distribute therapeutic compounds. Nanocarriers can transport therapeutic payloads directly to the affected regions of the HD brain by successfully bridging the blood-brain barrier. With the aid of nanotherapeutics, diagnostics drug research may transition from conventional to personalised treatment [6].

Epidemiology: The prevalence of Huntington's disease (HD) ranges between 10.6 and 13.7 cases per 100,000 individuals in Western countries [7]. One study reported that 3,763 individuals carry a 25% or 50% risk of developing HD, and 631 individuals have already been diagnosed. Based on this data, there could currently be around 4,700 individuals living with HD in Canada, with another 14,000 people at 50% risk. In the United States, the estimates suggest up to 43,000 diagnosed cases and approximately 123,000 individuals at 50% risk. This marks the first comprehensive study on HD epidemiology in Canada in over 30 years. Typically, HD results in death within 15–20 years after symptom onset [8, 9].

There is more than a tenfold regional variance in the global prevalence of HD. Even while Asian populations have a noticeably lower frequency, inconsistent case identification or diagnostic criteria may account for some of the difference. The prevalence of HD, a neurodegenerative disease that is extremely incapacitating, is roughly 0.40 per 100,000 in Asia as opposed to 5.70 per 100,000 in North America, Europe, and Australia. Regional variations in the occurrence of this inherited illness are largely due to variances in genetic haplotypes [9].

Causes: Using brain slices taken from people with different stages of Huntington's disease, researchers found an unexpected trend: as the disease progressed, the number of brain cells decreased exponentially, perhaps due to hereditary variables associated with neurodegeneration. The huntingtin (Htt) protein has an abnormally expanded polyglutamine (polyQ) tract as a result of the underlying genetic mutation that causes HD. The mutant Htt acquires toxic characteristics from this enlarged polyQ stretch, which aids in the advancement of neurodegeneration [9]. The mutant huntingtin protein (mHTT) misfolds in HD patients because of its extended polyglutamine sequence. This causes soluble HTT monomers to transform into oligomeric forms. The nucleus and cytoplasm also contain these oligomers, which serve as starting locations for the development of mHTT fibrils and bigger aggregates [8]. Neurodegeneration has been seen in animal models that express untranslated CAG-repeat RNA, and extensive research has shown that mHTT is toxic [10-17]. This suggests that mHTT RNA itself may have a pathogenic role [12].

Every single incidence of HD is caused by a genetic mutation that causes the HTT protein to abnormally expand a polyQ region. This enlargement gives HTT neurotoxic properties and raises the probability of HTT aggregation within cells [18, 19]. In addition, a variety of motor symptoms including chorea, myoclonus, stiffness, tremors, and dystonia have been documented in individuals with the C9orf72 expansion [19]. It is also common to associate HD etiology with the C9ORF72 gene's hexanucleotide repeat expansion [19-24]. It is well-known that oxidative stress and mitochondrial dysfunction play a crucial role in neuronal damage in Huntington's disease. Oxidative DNA damage and genomic instability at the huntingtin gene locus induce somatic CAG repeat expansion, one of the key drivers to HD development [25].

Pathogenesis: There are a number of pathways by which a huntingtin gene mutation causes neuronal malfunction and eventual death. Disruption of cellular homeostasis, neural transport, gene transcription, protein synthesis, mitochondrial integrity, and synaptic function are among the immediate impacts of the mutant huntingtin (mHTT) fragment at locus one, along with its potential to form hazardous aggregates [26-28]. Autophagy eliminates damaged organelles and protein aggregates, while the ubiquitin-proteasome pathway eliminates faulty proteins. These two systems are the main means by which cells breakdown proteins. Multiple biological systems may be affected by Huntington's disease (HD), according to research in both animal models and human tissues [28-34].

Both transcript variants encode the identical HTT protein; however, they differ in their 3′ untranslated regions (UTRs) by approximately 3 kb, resulting from alternative splicing of the HTT gene. The longer variation is mostly found in the brain, while the shorter transcript is expressed more widely. Postmortem HD brain samples and HD mice models have both shown the presence of truncated exon 1 transcripts, with the greatest expression detected in tissues with substantial CAG repeat expansions [35-37]. The nuclear pore complex (NPC) is a trio of nucleoporins (NUPs) that traverse the nuclear envelope and are essential for the transport of proteins and RNA from the nucleus to the cytoplasm. A major component of NPCs, NUP62, is mutated recessively in infants, leading to bilateral striatal necrosis. This suggests that malfunction of NPCs may contribute to the tissue-specific vulnerability observed in HD [38, 39]. In a mouse model of demyelination, the nuclear export inhibitor KPT-350 showed protective effects, and in a fruit fly model with 30 GGGGCC repetitions in C9orf72, a similar chemical likewise decreased neuronal damage [39-44].

The expansion of polyglutamine (polyQ) is involved in a wide variety of illnesses, however it is most commonly linked to a hazardous gain-of-function mechanism in neurological disorders. A subtype of spinocerebellar ataxia (SCA) has recently been discovered and is one of eight such variants. Another variant is associated with an expansion of CAG repeats in the THAP11 gene. Atrophy of the spinal cord and bulbar muscles, dentatorubral-pallidoluysian atrophy (DRPLA), and Huntington disease type 2 are further disorders linked to polyQ [45-47]. Alterations in HTT gene function are associated with pathological abnormalities in the cortex and striatum. The striatum has no capacity to produce its own brain-derived neurotrophic factor (BDNF) and must rely on its supply from the cortex for its survival. For BDNF synthesis and transport from the cortex to the striatum, the HTT protein is critical [48-51].

Transcriptional Dysregulation: A major factor in the development of Huntington's disease (HD) is deregulation of transcription. Important transcriptional regulators, such as p53, CREB-binding protein (CBP), and the cAMP response element-binding (CREB) protein, are disrupted by the mutant huntingtin protein (htt) [52-58]. On the other hand, wild-type htt helps regulate genes by bringing NRSE-binding transcription factors from the cytoplasm into the nucleus. The expression of genes containing NRSE is critical for the preservation of striatal neurons, and these factors play a pivotal role in this process [59].

Additionally, mutant htt interacts with molecular chaperones including the Hsp70 and Hsp40 families in polyQ-expanded proteins and colocalizes with protein aggregates. Impaired capacity to regulate aberrant protein folding results from a decrease in the number of available soluble forms of these chaperones when they get encased in aggregates [60-63].

Astrocytes and Microglial Dysfunction: Microglial dysfunction and astrocytes greatly affect Huntington's disease (HD)-related neuronal loss. Stimulating molecules via NF-κB signalling causes microglia to survey and increases PU1 and CCAT binding. Activated microglia can experience several polarisation states often known as M1 and M2 and these cells can move between them. Thought to be the principal initiators of the innate and adaptive immunological responses of the brain, M1 microglia are also linked to the inflammatory reaction. These phagocytic cells release cytotoxic compounds like quinolinic acid, ROS, and nitric oxide (NO), hence aggravating invasive infections [59, 64-70].

Defective Synaptic Transmission: Effective axonal transport is necessary for proper translocation to neuronal membranes, which facilitates synaptic transmission. Huntington's disease (HD) lowers synaptic excitability because neither GABAA (γ-aminobutyric acid type A) nor AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) receptors are supplied. HAP1 disrupts the connection between these receptors and the kinesin motor factor KIF5 by binding mutant huntingtin (htt) to this factor [59, 71-75].

Excitotoxicity and Medium Spiny Neurons (MSNs) Degeneration: The most obvious reduction is seen in MSNs located in the striatum. Furthermore, it has been demonstrated that glutamatergic inputs, which cause aberrant firing and neurotransmission, are particularly advantageous to MSNs. In a process known as excitotoxicity, glutamate can kill striatal neurones by activating NMDA receptors [76-80].

Pathogenic mHTT and Experimental Models for HD: The protein misfolds due to the enlarged polyQ region at the N-terminus of HTT, resulting in aberrant accumulations and aggregates. Inclusion bodies, which are present in the cytoplasm or nucleus, signify aggregated mHTT. A number of HD experimental models, such as those made from transgenic animals and human embryonic stem cells, have been created and studied in order to further HD research. These models display either full-length HTT or N-terminal segments of mHTT. Induced pluripotent stem cells produced from HD patients are also utilised [70, 81].

Symptoms: People have lower self-esteem, fear, and feelings of guilt. Apathy, not anxiety or depression, is the only emotional state associated with the progression of the illness [28]. Although the central nervous system (CNS) is the primary cause of Huntington's disease clinical symptoms, other factors such as hormone imbalances, weight loss, muscular atrophy, and metabolic abnormalities may also be important. Huntington's disease is thought to have a prodromal phase that begins long before a motor diagnosis can be made and is associated with neurobiological alterations such as striatal atrophy. Chora is typically the first motor symptom to be clinically detected, but bradykinesia and incoordination (or motor dysfunction) are typically more incapacitating [7, 82, 83]. Psychiatric disorders such as obsessive-compulsive disorder, sadness, anxiety, and irritability are linked to HD [83, 84]. Chora is one of the motor abnormalities caused by Huntington's disease, which disrupts the striatal output routes [85-87]. Additionally, apathy and weight loss have been connected to Huntington's disease [2, 28, 88].

Current Therapy: Due to the likelihood that the HD mutation is more prevalent and can mask Alzheimer's disease symptoms, neuropathological confirmation is essential for a conclusive diagnosis of co-existing Alzheimer's disease [28]. Clinical evaluation of Huntington's disease utilizes the Unified Huntington's Disease Rating Scale, which assesses motor deficits, behavioural symptoms, and cognitive impairments [89-91]. Recent advancements, such as the use of cryo-electron microscopy, have resolved the structure of the HTT protein, offering new insights into both the pathological mechanisms of HD and the normal biological functions of HTT [92].

Current therapeutic research in HD primarily focuses on targeting several mechanisms, including excitotoxicity, dopamine dysregulation, caspase activation, mutant huntingtin (mHTT) aggregation, mitochondrial abnormalities, transcriptional dysregulation, and dietary influences [93]. One promising approach under clinical investigation is antisense oligonucleotide (ASO) therapy. Small molecule splicing modulators, RNA interference (RNAi), and ASOs are being explored for their RNA-targeting capabilities. A phase 1b/2a clinical trial is presently evaluating ASOs in HD patients [94-96]. Tetrabenazine, a dopamine-depleting agent, is considered effective for managing chorea, although it may be associated with significant adverse effects. Newer antipsychotics such as aripiprazole and olanzapine are being utilized for managing chorea and psychosis, offering improved safety profiles compared to older medications [97-99]. Deutetrabenazine, a deuterated analog of tetrabenazine, has shown enhanced pharmacokinetics with a longer half-life and reduced variability. Findings from the FIRST-HD trial demonstrate that deutetrabenazine effectively reduces chorea and improves motor symptoms over a 12-week period [100-103].

Various biomarkers are implicated in HD pathophysiology, including oxidative stress markers like 8-OHdG; metabolic markers such as creatine kinase and branched-chain amino acids; cholesterol derivatives like 24-OH cholesterol; and immune mediators such as clusterin, complement proteins, and interleukins 6 and 8. Other indicators include transcriptional changes, endocrine hormones (e.g., cortisol, leptin, and ghrelin), brain-derived neurotrophic factor (BDNF), and adenosine 2A receptors [104-108]. Imaging and structural biomarkers useful for early HD detection and progression tracking include striatal volume, cortical thickness, subcortical white matter volume, total brain and ventricular size, functional MRI, PET scans using fluorodeoxyglucose, and magnetic resonance spectroscopy measuring lactate levels [108-112]. In addition, early detection may benefit from quantitative motor assessments, neurophysiological evaluations (e.g., transcranial magnetic stimulation), and precise eye movement analyses [113, 114].

An increase in BDNF levels was found to be concentration-dependent in striatal tissues of both N171-82Q HD mouse models and wild-type striatal cells, suggesting that glatiramer acetate could emerge as a future HD treatment option [115-117]. In a randomized controlled trial, the antipsychotic sulpiride demonstrated effectiveness in reducing chorea symptoms [98, 118]. Cholinesterase inhibitors such as galantamine, donepezil, and rivastigmine have shown positive results in two randomized trials for HD treatment [119]. Pharmacological options also include SSRIs like citalopram, fluoxetine, paroxetine, and sertraline, along with dual-action antidepressants such as mirtazapine and venlafaxine. Antipsychotic medications are used to address psychosis and aggressive behavior, while drugs like methylphenidate, atomoxetine, modafinil, amantadine, bromocriptine, and bupropion have been explored for managing apathy, although robust evidence from randomized trials remains limited [120].

Caspases 1 and 2 are recognized as key contributors in HD pathology. Minocycline has shown therapeutic promise by reducing the expression of inducible nitric oxide synthase, inhibiting the upregulation of caspase-1 and caspase-3 mRNA, and slowing disease progression [121]. Amantadine has been found effective for treating HD-related chorea [122-124], and for idiopathic dystonia, treatments may involve botulinum toxin, benzodiazepines, and baclofen [121]. Another trial also supports the use of amantadine for controlling chorea in HD [124]. In the 3-nitropropionic acid (3NP) model of HD, memantine has shown neuroprotective effects by decreasing striatal damage, reducing Bax expression, increasing Bcl-xl, preserving body weight, and minimizing lesion volume, likely through inhibition of calpain activity [125, 126]. Congo red has shown potential for symptom relief in HD by modifying protein misfolding and aggregation, thereby reducing toxic oligomers and enhancing motor performance [127, 128]. The rapamycin analog CCI-779, which inhibits mTOR, promotes autophagy, counteracts polyglutamine toxicity, and reduces protein aggregate formation, making it a promising therapeutic candidate for HD management [129-132].

TABLE 1: CURRENT TREATMENT OPTIONS AVAILABLE FOR HUNTINGTON DISEASE

Drug	Animal/Cell	Dose	Uses	Mechanism	Refe.
Glatiramer acetate	HD transgenic and wild-type mice	(1.5 to1.7mg/mouse) for five days.	immunomodulatory agents	Increases BDNF protein levels0	115-117, 133
Deutetrabenazine	Men and women (Randomized controlled trial)	mean (SD) dose was 39.7 mg (9.3 mg; range, 12-48 mg) in the deutetrabenazine group and 43.3 mg (7.6 mg; range, 12-48 mg) in the placebo group.	Chorea	Vesicular monoamine transporter (VMAT) 2 inhibitor	100-103
Sulpiride	Randomized controlled trial (RCT)	300 mg/day, increased with 300 mg each week (max 1200 mg/day)2 * 4 weeks, 1 week washout	Atypical Antipsychotics	Selective D2 & D3 antagonist	13498, 118
Bupropion	-	3 months of receiving 300 mg	Atypical antidepressant	Selective serotonin reuptake	120

		per day bupropion		inhibitor (SSRI)	
Minocycline	R6/2 mouse model	At 6 weeks age, either saline, minocycline hydrochloride (5 mg/kg), or with tetracycline hydrochloride (5 mg/kg) in 0.5 ml of saline.	Tetracycline antibiotic	inhibits caspase-1 and caspase-3 mRNA upregulation, reduces nitric oxide synthetase activity.	121, 135
Amantadine	RCT	ceiling dose of amantadine was 300mg in 6 weeks	Dopaminergic agent, Dyskinesia	Upregulate tyrosine hydroxylase (TH), σ1 receptor agonist	122, 123, 136
Amantadine	RCT	amantadine hydrochloride, 100 mg 3 times daily for 2 weeks, and placebo for 2 weeks.	Dopaminergic agent, Dyskinesia	Upregulate tyrosine hydroxylase (TH), σ1 receptor agonist	123, 137
Memantine	Rats	Either memantine (20 mg/kg/day) or PBS for five days with 3NP continuous infusion	Improved cognition, mood behaviour	AChE inhibitor, NMDA receptors anatagonist, high D2 receptor agonist, sigma σ1 receptor agonist	125, 126, 138
Rapamycin	cell models, transgenic mice and human brain	1 μM rapamycin or DMSO	induces autophagy and reduces toxicity of polyglutamine expansions	mTOR inhibitor	130-132, 139

Nanotherapy: Due to their high surface area-to-mass ratio, nanoparticles possess unique optical, magnetic, and biological properties within biological systems. They can be broadly categorized as organic (e.g., liposomes) or inorganic (e.g., gold nanoparticles). Polymeric nanoparticles, made from biodegradable and biocompatible polymers, are particularly effective in protecting drugs from degradation. Additionally, nanoparticles enable the delivery of poorly water-soluble drugs with low bioavailability [140]. These nanocarriers can transport a range of therapeutic agents including siRNAs, stem cells, neurotrophic factors, and pharmaceuticals. Various nanoparticle types such as solid lipid, polymeric, lipid-based, liposomal, and metal/metal oxide nanoparticles are being explored for treating Huntington's disease (HD). Integrating nanomaterials with stem cell systems enhances neural stem cell (NSC) expansion, targeted delivery of bioactive molecules, and allows for noninvasive, long-term monitoring of cell movements post-implantation. Merging nanotechnology, stem cell therapy, and molecular biology may improve the efficacy of these treatments while addressing existing limitations [141]. W20-SPIONs have been able to cross the blood-brain barrier and specifically bind to oligomeric regions, producing MRI signals in transgenic mice, and thereby differentiating between Parkinson's and Huntington's disease. This makes them promising diagnostic tools for HD [142]. Since mitochondrial dysfunction plays a central role in HD, nanoparticle-based theranostic systems are being explored as potential therapeutic interventions [143]. The CRISPR/Cas system also holds promise in gene editing strategies aimed at treating monogenic disorders like HD, especially through targeting repeated RNA sequences (e.g., CAGN repeats) using R-Cas9 [144].

In HD rat models, intravenous administration of human immature dental pulp stem cells (hIDPSCs) helped restore BDNF, DARPP32, and D2R levels, enhancing neurogenesis and neuroprotection [145]. Targeting multiple cellular, epigenetic, and genetic mechanisms may offer more comprehensive symptom relief. For instance, human striatal organoids (hStrOs) derived from hiPSCs mimic early brain development and integrate effectively into host neuronal circuits post-transplantation [146, 147]. Co-transplantation of hStrOs with human umbilical cord-derived mesenchymal stem cells

(hUC-MSCs) mitigates immune rejection and mechanical trauma by leveraging the immunomodulatory and neurotrophic functions of hUC-MSCs [147, 148]. Theranostic approaches that combine drug-free photothermal therapy with advanced imaging to monitor aggregate ablation support the potential of aggregate-disrupting strategies in treating neurodegenerative diseases like HD [149].

Pre-treatment with sesamol (5, 10, and 20 mg/kg) improved oxidative damage markers, behaviour, and mitochondrial enzyme activities. At higher doses, sesamol increased cell survival, indicating its potential therapeutic role in HD due to its antioxidant properties [150]. Selenium nanoparticles (Nano-Se) were found to reduce neuronal death and behavioural impairment at low doses in HD models, including in C. elegans, highlighting their therapeutic promise [151]. In HD animal models, hybrid-g7-NPs-chol, containing deuterium-labeled cholesterol, delivered cholesterol in a controlled, inflammation-free manner, restoring natural cholesterol synthesis and improving motor and cognitive deficits [152]. Dual dosing of hybrid-g7-NPs-chol produced lasting improvements in cognition, behaviour, and brain pathology [153].

A promising delivery strategy includes nasal administration of chitosan nanoparticles loaded with anti-HTT siRNA, effectively suppressing mutant HTT expression and contributing to HD management [154]. In a 3NP-induced HD rat model, solid lipid nanoparticles loaded with rosmarinic acid (SLNPRT) showed significant behavioural improvements and antioxidant effects, pointing to their therapeutic value [155]. Both rat striatal cells (ST14A-HTT120Q) and human HD fibroblasts displayed reduced HTT expression after treatment with CDsiRNA nanoparticle complexes. In the R6/2 HD mouse model, a single injection of these nanoparticles resulted in prolonged gene silencing, and multiple injections further improved motor functions [156-158].

Engineered γ-Fe_2O_3 poly(trehalose) nanoparticles were 1,000–10,000 times more effective than plain trehalose in preventing extracellular fibril formation, inhibiting mHTT aggregation in neurons, and reducing aggregates in HD mouse brains [159]. In 3NP-induced HD models, curcumin encapsulated in solid lipid nanoparticles (CSLNs) significantly decreased mitochondrial swelling, reactive oxygen species, protein carbonyls, and lipid peroxidation, while enhancing antioxidant enzyme activity such as superoxide dismutase and glutathione [160-164]. Similarly, low doses of thymoquinone in suspension lipid nanoparticles (TQ-SLN) were effective in reversing behavioural, biochemical, and histopathological changes in HD models [165-167].

Chitosan nanoparticles enhanced with ginger extract showed efficacy in 3NP-induced HD rat models by improving cognitive and motor functions (e.g., grip strength, gait, memory) and by reducing oxidative stress markers like malondialdehyde and protein carbonyls. These effects were accompanied by increases in antioxidants such as glutathione, catalase, and superoxide dismutase. Inhibition of acetylcholine esterase was also associated with improved cognition [168]. Ginger, known for its neuroprotective properties, has limited bioavailability and brain penetration, but nanoparticle formulations can overcome these barriers. Finally, PLGA nanoparticles carrying PGQ9P2, QBP1, and NT17 peptides were shown to significantly reduce polyglutamine aggregation in neuronal models (Neuro 2A, PC12) and enhance motor performance post-treatment [169].

TABLE 2: THE NANOTECHNOLOGY-BASED OPTIONS AVAILABLE FOR HUNTINGTON DISEASE

Drug	Animal/Cell/Model	Dose	Effect	Mechanism	Ref.
Sesamol nano-formulation	Wistar rats	sesamol (10, and 20 mg/kg)	Mitochondrial improvement	Decreased neuroinflammation	150
Se-NP	transgenic HD models of Caenorhabditis elegans (C. elegans)	0.02, 0.2, and 2 μM Se-NP	Decreases behavioural dysfunction	Decrease ROS, inhibits the aggregation of huntingtin proteins, downregulate the expression of histone deacetylase family members at mRNA levels	151

Hybrid-g7-NPs-chol	R6/2 miceMice	25 mg D6 Chol, 20 mg PLGA, 5 mg PLGA-g7	Improved motor function	Increased cholesterol content in brain	[152]
Chitosan nanoparticle loaded with siRNA	female YAC128 transgenic mice.	6 µL NP, size (100-160 nm)	Reduced mHTTgene expression	HTT silencing	[154]
SLNPRT loaded with Rosmarinic acid	Male Wistar rat	RA (12 mg), 3-NP (10 mg/kg), SLNPRT (i.v. 12 mg, SLN)	Improved behavioural dysfunction	Decrease ROS	[155]
CD·siRNA nanoparticles	Rat striatal cells (ST14A-HTT120Q) and human HD primary fibroblasts	100 nM siRNA	Improved motor dysfunction	HTT gene silencing RNA based gene therapy	[156,157,170]
γ-Fe2O3 poly(trehalose) nanoparticles	HD150Q cell line	poly(trehalose) nanoparticles (0.4 mg/mL, corresponding to 50 µM trehalose)	Reducing mutant huntingtin aggregates	inhibiting protein fibrillation	[159]
CSLNs	Wistar rats	20 mg/kg 3-NP, 40 mg/kg C-SLN for 7 days	Enhanced antioxidant activity	Decreased mitochondrial swelling, ROS, protein carbonyl & lipid peroxidation	[101][160-164]
TQ-SLNs	Wistar rats	TQ-SLNs (10 and 20 mg/kg) and TQ-S (80 mg/kg)	Restore antioxidant defense system	Mitochondrial SDH inhibition and alleviates anti-cholinergic effect	[165]
Ginger-loaded chitosan nanoparticles	Wistar rats	normal saline treatment (i. p.), (10 mg/kg, i. p.) +3-NP (10 mg/kg, i. p.)	Cognitive improvement	Inhibition of the acetylcholine esterase enzyme	[168]
PLGA loaded nanoparticles containing PGQ9P2, QBP1, and NT17	Neuro 2A and PC12 cell	1 & 3 µg/mg for QBP1-NPs and NT17-NPs	Improved motor performance	Reduction in polyglutamine aggregation	[104]

Future-outlook: Nanotherapeutics offer promising advantages in treating Huntington's disease (HD) by enabling targeted drug delivery across the blood–brain barrier (BBB), directly reaching the affected brain regions. This approach enhances therapeutic outcomes and reduces adverse effects. Additionally, nanotherapeutics are being explored as diagnostic tools in HD management. The rapid growth in this field opens up numerous possibilities for transforming HD treatment. However, current challenges remain, such as the absence of FDA-approved nanotherapeutic options for HD and the necessity for comprehensive safety evaluations. By targeting key pathological factors such as mHTT DNA, mHTT RNA, mutant protein, mitochondrial dysfunction, defective autophagy, cell death pathways, and histone methylation, nanotherapeutic platforms help mitigate HD progression [6]. To validate the impact of nanoparticles in human systems, clinical studies are essential. Since most investigations focus on how nanoparticles influence metabolic activity, it is crucial to conduct in vivo studies to better understand their physical, chemical, and metabolic characteristics. Further insights into the mechanisms that allow nanoparticles to traverse physiological barriers *in-vivo* will be instrumental in refining their design. Establishing standardized criteria to assess the biodegradability of nanoparticles in vivo is also critical. Therefore, fundamental research is required before nanotechnology can be routinely applied in clinical practice. Expanding interdisciplinary research will contribute to the development of an integrated nanotechnology-based therapeutic strategy for neurodegenerative diseases (NDs) [143]. Future efforts should prioritize the integration of multimodal data and rigorous clinical validation to enhance model performance. Leveraging machine learning for HD diagnosis holds potential for earlier interventions,

individualized therapies, and improved outcomes for patients and their families [171]. Gene therapy is a promising avenue for future HD treatments, with the goal of directly correcting or silencing the mutant HTT gene or associated DNA damage response (DDR) mechanisms. A combined strategy involving gene and cell therapy entails replacing damaged neurons with striatal organoids derived from iPSCs, either from healthy donors or gene-corrected HD patients. To reduce immune responses and injection-related inflammation during transplantation, mesenchymal stem cells (MSCs) are co-transplanted. These MSCs also facilitate BDNF production, which may support neuronal survival and recovery. Additionally, microglial repopulation creates a more favorable environment for the engraftment and differentiation of transplanted cells. Going forward, research should focus on establishing the safety, therapeutic efficacy, and clinical utility of these organoid-based therapies in animal models of HD [147]. The Huntington's Disease Integrated Staging System (HD-ISS) provides a framework for classifying individuals based on clinical, biological, and functional indicators. Starting from Stage 0 which includes individuals genetically predisposed to HD but showing no clinical manifestations the HD-ISS outlines a progressive staging model: Stage 1 (biological markers of disease), Stage 2 (appearance of clinical symptoms), and Stage 3 (functional decline). Each stage is defined by precise, evidence-based thresholds, facilitating accurate staging for research and clinical monitoring [83].

TABLE 3: ONGOING CLINICAL RESEARCH CONTINUES TO TACKLE THE VARIOUS CHALLENGES ASSOCIATED WITH HD TREATMENT. A SUMMARY OF THESE CLINICAL INVESTIGATIONS IS PROVIDED IN

NCT	Drug/Agent	Phase	Dose	Population	Study design	Mechanism	Outcome/Effect
NCT03252535	Cellavita HD	II	1x10^6 & 2x10^6 cells/weight every 30 days (total 3 cycle) respectively	N = 35	Randomized, DBPC, parallel study	stem cell therapy	UHDRS
NCT05475483	SOM3355 (Bevantolol hydrochloride)	IIb	up-titration for 2 weeks of 200 mg& 300 mg (twice daily) given for 8 additional weeks, and down-titration for 2 weeks respectively	N = 140	Randomized controlled study (RCT)	β1-adrenoreceptor antagonist, vesicular monoamine transporter type 2 inhibitor	Efficacy & safety
NCT03761849	RO7234292(Tominersen)	III	RO4234292x120 mg is administered intrathecally every 8 weeks& 16 weeks respectively	N = 899	Randomized controlled study (RCT)	ASO-mediated non-allele-specific degra--dation of HTT mRNA	Efficacy, safety, and biomarker effects (UHDRS, TFC)
NCT04000594	RO7234292(Tominersen)	I	dose level 1 of 30 mg, dose level 2 of 60 mg & dose level 3 of 120 mg on Day 1 & Day 29 each respectively.	N = 12	adaptive multiple-dose clinical study, non-randomized controlled study, Parallel study	ASO-mediated non-allele-specific degra -dation of HTT mRNA	Safety & tolerability
NCT04556656	Pridopidine	III	Pridopidine 45mg twice daily (BID)	N = 499	Randomized controlled study (RCT)	Sigma-1 Receptor agonist	Safety & efficacy Change in UHDRS, TFC
NCT05655520	SAGE-718	III	Cohort 1 (Direct rollover ≤7 days), Cohort 2 (Gap rollover >7 days),	N = 300	non-randomized controlled study	Active allosteric NMDA receptor modulator	Safety and tolerability

			Cohort 3 (De novo) from Day 1 up to Month 48 respectively.				
NCT02336633	Resveratrol	-	80mg/day) every day for 1 year	N = 102	RCT, parallel	Antioxidant, Cox-1 inhibitor	Change in caudate volume
NCT06444217	Gene therapy	Recruiting	Procedure- Skin biopsy	N = 20	Open label, single group	Gene therapy	Development & validation of RNA trans-splicing gene therapy
NCT04713982	Deutetrabenaz-ine (Austedo)	II & III	Starting dose of 6mg/day & up-titrated in increments of 6mg/day per week up to 600 mg per day, oral capsules for 8 weeks	N = 30	Open label, single group	VMAT2 inhibitor	SIT & MSE
NCT00980694	Ubiquinol	I		N = 6	Open label, single group	Co-enzyme Q10	serum coenzyme Q10 levels
NCT02453061	Triheptanoin	II	Triheptanoin oil orally administered at 1g/kg/day for 12 months	N = 100	RCT, parallel study	Anaplerotic Therapy	Efficacy in TRIHEP3, Neuroimaging biomarker
NCT04515550	Mitochondrial metabolomics biomarkers	Observational	18 months target follow-up	N = 27	Cohort study	Lumbar puncture analysis	Change in UHDRS & MoCA
NCT06585449	ALN-HTT02	I	Single dose of ALN-HTT02 during the Double-blind Part of the study.	N = 54	RCT, parallel study	Novel C16-siRNA Conjugate for HTT-lowering in the CNS	Safety, Tolerability, Pharmacokinetic &Pharmacodyna-mics
NCT05541627	AB-1001	I & II	One-time intracerebral bilateral injections of AB-1001 (AAVrh10.CAG.hCYP46A1), an adeno-associated viral vector serotype Rh10 containing the human cholesterol 24-hydroxylase gene for 52 weeks	N = 5	Non-randomized, open label, sequential study	Gene therapy	Safety, tolerability, and preliminary efficacy of AB-1001
NCT06254482	PTC518	II	PTC518 5 mg,10 mg& 20 mg tablets once daily orally for 24 months respectively	N = 250	RCT, parallel study	Lower mHTT protein	long-term safety and pharmacodynamic effects
NCT04478734	Combination of Thiamine and Biotin	II	Thiamine 600 mg every day + Biotin 150mg every day & Thiamine 1200 mg every day + Biotin 300mg every day for	N = 24	RCT, parallel, open label study	Combined oral thiamine and biotin therapy	safety and tolerability

			52 weeks				
NCT06469853	MBF-015	II	16 mg & 32 mg oral capsules respectively for 28 days	N = 10	Non-randomized, open label study	CoREST/HDAC1/2 inhibitor	Safety and efficacy of daily MBF-015
NCT05032196	WVE-003	Ib & IIa	Dose A, B & C respectively	N = 47	RCT, sequential study	stereopure antisense oligonucleotide (ASO)	Safety, tolerability, PK, and PD
NCT01458470	Memantine	II	1 BID for 24 weeks	N = 19	RCT, parallel study	NMDA Receptor Antagonist	Utility of TRACK-HD study endpoints
NCT02535884	Deep brain stimulaton	-	Device: ACTIVA® PC neurostimulator (Model 37601)	N = 48	RCT, parallel study, Open label surgery with randomized sham stimulation	DBS	UHDRS
NCT02197130	PF-02545920	II	5mg BID for 7 days, 10mg BID for 7 days, 15 mg BID for 7 days and 20 mg BID to week 26	N = 272	RCT, parallel study	PDE10A inhibitor	Change in UHDRS

CONCLUSION: Nanotherapeutics possess the capability to cross the blood–brain barrier (BBB) effectively, allowing for the direct delivery of therapeutic agents to the regions of the brain affected by Huntington's disease (HD), thereby reducing side effects and improving treatment outcomes [6]. While current therapies primarily address symptoms, RNA interference (RNAi)-based nanotherapeutics have emerged as innovative tools for modulating stem cell behavior both *in-vitro* and *in-vivo*. Compared to traditional techniques such as lipoplex transfection, electroporation, and lentiviral methods, nano- and microcarriers used for nucleotide delivery offer considerable advantages [172]. Due to their unique physicochemical properties, nanoparticles are highly suitable for targeted drug delivery and offer neuroprotective potential. Their ability to traverse the BBB supports the development of precision medicine approaches [173]. Nanocarriers functionalized with targeting elements such as proteins, peptides, aptamers, or cell membrane-derived vesicles can actively engage antigen-presenting cells (APCs), enhancing delivery specificity [174]. Furthermore, exosomes present dual utility: they can be used as carriers in gene-silencing therapies and also serve as biomarker sources for early-stage disease detection, thereby contributing to our understanding of HD pathogenesis [175]. With promising results demonstrated in preclinical settings, strategies involving genetic, epigenetic, and stem cell-based interventions hold great potential for future clinical applications. Continued development of these therapeutic avenues could ultimately pave the way for a cure for this devastating neurodegenerative condition [176].

ACKNOWLEDGEMENT: Nil

CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Dugger BN and Dickson DWJCSHpib: Pathology of neurodegenerative diseases 2017; 9: 028035.
2. Bates GP, Dorsey R, Gusella JF, Hayden MR, Kay C, Leavitt BR, Nance M, Ross CA, Scahill RI and Wetzel RJNrDp: Huntington disease 2015; 1: 1-21.
3. Martí EJBP: RNA toxicity induced by expanded CAG repeats in H untington's disease 2016; 26: 779-786.
4. Wright GE, Collins JA, Kay C, McDonald C, Dolzhenko E, Xia Q, Bečanović K, Drögemöller BI, Semaka A and Nguyen CMJTAJoHG: Length of uninterrupted CAG, independent of polyglutamine size, results in increased somatic instability, hastening onset of Huntington disease 2019; 104: 1116-1126.
5. Caron NS, Dorsey ER and Hayden MRJNRDD: Therapeutic approaches to Huntington disease: from the bench to the clinic, 2018; 17: 729-750.
6. Khan S, Bano N, Ahamad S, Dar NJ, Nazir A and Bhat SAJCCR: Advances in nanotherapeutic strategies for Huntington's disease: Design, delivery, and neuroprotective mechanisms 2025; 522: 216206.

7. McColgan P and Tabrizi SJJEjon: Huntington's disease: a clinical review 2018; 25: 24-34.
8. Medina A, Mahjoub Y, Shaver L and Pringsheim TJMd: Prevalence and incidence of Huntington's disease: an updated systematic review and meta-analysis, 37, 2022, 2327-2335.
9. Rawlins MD, Wexler NS, Wexler AR, Tabrizi SJ, Douglas I, Evans SJ and Smeeth LJN: The prevalence of Huntington's disease, 46, 2016, 144-153.
10. Loupe JM, Pinto RM, Kim K-H, Gillis T, Mysore JS, Andrew MA, Kovalenko M, Murtha R, Seong I and Gusella JFJHmg: Promotion of somatic CAG repeat expansion by Fan1 knock-out in Huntington's disease knock-in mice is blocked by Mlh1 knock-out, 29, 2020, 3044-3053.
11. Niso-Santano M, Fuentes JM and Galluzzi LJCD: Immunological aspects of central neurodegeneration, 10, 2024, 41.
12. Lee J-M, Wheeler VC, Chao MJ, Vonsattel JPG, Pinto RM, Lucente D, Abu-Elneel K, Ramos EM, Mysore JS and Gillis TJC: Identification of genetic factors that modify clinical onset of Huntington's disease, 162, 2015, 516-526.
13. Lee J-M, Correia K, Loupe J, Kim KH, Barker D, Hong EP, Chao MJ, Long JD, Lucente D and Vonsattel JPGJC: CAG repeat not polyglutamine length determines timing of Huntington's disease onset, 178, 2019, 887-900. e814.
14. Lieberman AP, Shakkottai VG and Albin RLJARoPMoD: Polyglutamine repeats in neurodegenerative diseases, 14, 2019, 1-27.
15. Ciosi M, Maxwell A, Cumming SA, Moss DJH, Alshammari AM, Flower MD, Durr A, Leavitt BR, Roos RA and Holmans PJE: A genetic association study of glutamine-encoding DNA sequence structures, somatic CAG expansion, and DNA repair gene variants, with Huntington disease clinical outcomes, 48, 2019, 568-580.
16. Moss DJH, Pardiñas AF, Langbehn D, Lo K, Leavitt BR, Roos R, Durr A, Mead S, Coleman A and Santos RDJTLN: Identification of genetic variants associated with Huntington's disease progression: a genome-wide association study, 16, 2017, 701-711.
17. Goold R, Flower M, Moss DH, Medway C, Wood-Kaczmar A, Andre R, Farshim P, Bates GP, Holmans P and Jones LJHmg: FAN1 modifies Huntington's disease progression by stabilizing the expanded HTT CAG repeat, 28, 2019, 650-661.
18. Koutsis G, Karadima G, Kartanou C, Kladi A and Panas MJNoa: C9ORF72 hexanucleotide repeat expansions are a frequent cause of Huntington disease phenocopies in the Greek population, 36, 2015, 547. e513-547. e516.
19. Ida CM, Butz ML, Lundquist PA and Dawson DBJND: C9orf72 repeat expansion frequency among patients with Huntington disease genetic testing, 18, 2019, 239-253.
20. Alva-Diaz C, Alarcon-Ruiz CA, Pacheco-Barrios K, Mori N, Pacheco-Mendoza J, Traynor BJ, Rivera-Valdivia A, Lertwilaiwittaya P, Bird TD and Cornejo-Olivas MJFiG: C9orf72 hexanucleotide repeat in huntington-like patients: systematic review and meta-analysis, 11, 2020, 551780.
21. Martins J, Damásio J, Mendes A, Vila-Chã N, Alves JE, Ramos C, Cavaco S, Silva J, Alonso I and Magalhães MJNS: Clinical spectrum of C9orf72 expansion in a cohort of Huntington's disease phenocopies, 39, 2018, 741-744.
22. Van Mossevelde S, van der Zee J, Cruts M and Van Broeckhoven CJCoig: development, Relationship between C9orf72 repeat size and clinical phenotype, 44, 2017, 117-124.
23. Konopka A and Atkin JDJIjoms: The emerging role of DNA damage in the pathogenesis of the C9orf72 repeat expansion in amyotrophic lateral sclerosis, 19, 2018, 3137.
24. Estevez-Fraga C, Magrinelli F, Hensman Moss D, Mulroy E, Di Lazzaro G, Latorre A, Mackenzie M, Houlden H, Tabrizi SJ and Bhatia KPJNG: Expanding the spectrum of movement disorders associated with C9orf72 hexanucleotide expansions, 7, 2021, e575.
25. Mätlik K, Baffuto M, Kus L, Deshmukh AL, Davis DA, Paul MR, Carroll TS, Caron M-C, Masson JY and Pearson CEJNg: Cell-type-specific CAG repeat expansions and toxicity of mutant Huntingtin in human striatum and cerebellum, 56, 2024, 383-394.
26. Wild EJ and Tabrizi SJJTLN: Therapies targeting DNA and RNA in Huntington's disease, 16, 2017, 837-847.
27. Plotkin JL, Surmeier DJJCoin, Corticostriatal synaptic adaptations in Huntington's disease, 33, 2015, 53-62.
28. Andhale R, Shrivastava DJC, Huntington's disease: a clinical review, 14, 2022.
29. Liu Q, Cheng S, Yang H, Zhu L, Pan Y, Jing L, Tang B, Li S, Li X-JJPotNAoS, Loss of Hap1 selectively promotes striatal degeneration in Huntington disease mice, 117, 2020, 20265-20273.
30. Wang Y, Le W-DJAb, science db, Autophagy and ubiquitin-proteasome system, 2019, 527-550.
31. Sahoo S, Padhy AA, Kumari V, Mishra PJMN, Role of ubiquitin–proteasome and autophagy-lysosome pathways in α-synuclein aggregate clearance, 59, 2022, 5379-5407.
32. Dikic IJArob, Proteasomal and autophagic degradation systems, 86, 2017, 193-224.
33. Blasiak J, Pawlowska E, Szczepanska J, Kaarniranta KJIjoms, Interplay between autophagy and the ubiquitin-proteasome system and its role in the pathogenesis of age-related macular degeneration, 20, 2019, 210.
34. Le Guerroué F, Youle RJJCD, Differentiation, Ubiquitin signaling in neurodegenerative diseases: an autophagy and proteasome perspective, 28, 2021, 439-454.
35. Neueder A, Landles C, Ghosh R, Howland D, Myers RH, Faull RL, Tabrizi SJ, Bates GPJSr, The pathogenic exon 1 HTT protein is produced by incomplete splicing in Huntington's disease patients, 7, 2017, 1307.
36. Fienko S, Landles C, Sathasivam K, McAteer SJ, Milton RE, Osborne GF, Smith EJ, Jones ST, Bondulich MK, Danby ECJB, Alternative processing of human HTT mRNA with implications for Huntington's disease therapeutics, 145, 2022, 4409-4424.
37. Podvin S, Reardon HT, Yin K, Mosier C, Hook VJJon, Multiple clinical features of Huntington's disease correlate with mutant HTT gene CAG repeat lengths and neurodegeneration, 266, 2019, 551-564.
38. Beck M, Hurt EJNrMcb, The nuclear pore complex: understanding its function through structural insight, 18, 2017, 73-89.
39. Zhang K, Donnelly CJ, Haeusler AR, Grima JC, Machamer JB, Steinwald P, Daley EL, Miller SJ, Cunningham KM, Vidensky SJN, The C9orf72 repeat expansion disrupts nucleocytoplasmic transport, 525, 2015, 56-61.
40. Jovičić A, Mertens J, Boeynaems S, Bogaert E, Chai N, Yamada SB, Paul III JW, Sun S, Herdy JR, Bieri GJNn, Modifiers of C9orf72 dipeptide repeat toxicity connect nucleocytoplasmic transport defects to FTD/ALS, 18, 2015, 1226-1229.
41. Freibaum BD, Lu Y, Lopez-Gonzalez R, Kim NC, Almeida S, Lee K-H, Badders N, Valentine M, Miller BL, Wong PCJN, GGGGCC repeat expansion in C9orf72

compromises nucleocytoplasmic transport, 525, 2015, 129-133.
42. Yuva-Aydemir Y, Almeida S, Krishnan G, Gendron TF, Gao F-BJNc, Transcription elongation factor AFF2/FMR2 regulates expression of expanded GGGGCC repeat-containing C9ORF72 allele in ALS/FTD, 10, 2019, 5466.
43. McGoldrick P, Lau A, You Z, Durcan TM, Robertson JJCR, Loss of C9orf72 perturbs the Ran-GTPase gradient and nucleocytoplasmic transport, generating compositionally diverse Importin β-1 granules, 42, 2023.
44. Zhu Q, Jiang J, Gendron TF, McAlonis-Downes M, Jiang L, Taylor A, Diaz Garcia S, Ghosh Dastidar S, Rodriguez MJ, King PJNn, Reduced C9ORF72 function exacerbates gain of toxicity from ALS/FTD-causing repeat expansion in C9orf72, 23, 2020, 615-624.
45. Stoyas CA, La Spada ARJHocn, The CAG–polyglutamine repeat diseases: a clinical, molecular, genetic, and pathophysiologic nosology, 147, 2018, 143-170.
46. Paulson HL, Shakkottai VG, Clark HB, Orr HTJNRN, Polyglutamine spinocerebellar ataxias—from genes to potential treatments, 18, 2017, 613-626.
47. Tan D, Wei C, Chen Z, Huang Y, Deng J, Li J, Liu Y, Bao X, Xu J, Hu ZJMD, CAG repeat expansion in THAP11 is associated with a novel spinocerebellar ataxia, 38, 2023, 1282-1293.
48. Yu C, Li CH, Chen S, Yoo H, Qin X, Park HJSr, Decreased BDNF release in cortical neurons of a knock-in mouse model of Huntington's disease, 8, 2018, 16976.
49. Vitet H, Brandt V, Saudou FJCOiN, Traffic signaling: new functions of huntingtin and axonal transport in neurological disease, 63, 2020, 122-130.
50. Hong Y, Zhao T, Li X-J, Li SJJoN, Mutant huntingtin impairs BDNF release from astrocytes by disrupting conversion of Rab3a-GTP into Rab3a-GDP, 36, 2016, 8790-8801.
51. Speidell A, Bin Abid N, Yano HJB, Brain-derived neurotrophic factor dysregulation as an essential pathological feature in Huntington's disease: mechanisms and potential therapeutics, 11, 2023, 2275.
52. Bäuerlein FJ, Saha I, Mishra A, Kalemanov M, Martínez-Sánchez A, Klein R, Dudanova I, Hipp MS, Hartl FU, Baumeister WJC, In situ architecture and cellular interactions of PolyQ inclusions, 171, 2017, 179-187. e110.
53. Adegbuyiro A, Sedighi F, Pilkington IV AW, Groover S, Legleiter JJB, Proteins containing expanded polyglutamine tracts and neurodegenerative disease, 56, 2017, 1199-1217.
54. Fusco FR, Paldino EJPCf, diseases, Role of phosphodiesterases in Huntington's disease, 2017, 285-304.
55. Khakha N, Khan H, Kaur A, Singh TGJPR, Therapeutic implications of phosphorylation-and dephosphorylation-dependent factors of cAMP-response element-binding protein (CREB) in neurodegeneration, 75, 2023, 1152-1165.
56. Sharma S, Taliyan RJPr, Transcriptional dysregulation in Huntington's disease: the role of histone deacetylases, 100, 2015, 157-169.
57. Valor LMJMn, Transcription, epigenetics and ameliorative strategies in Huntington's Disease: a genome-wide perspective, 51, 2015, 406-423.
58. Jurcau AJB, Molecular pathophysiological mechanisms in Huntington's disease, 10, 2022, 1432.
59. Irfan Z, Khanam S, Karmakar V, Firdous SM, El Khier BSIA, Khan I, Rehman MU, Khan AJBS, Pathogenesis of Huntington's disease: an emphasis on molecular pathways and prevention by natural remedies, 12, 2022, 1389.
60. Chen JY, Parekh M, Seliman H, Bakshinskaya D, Dai W, Kwan K, Chen KY, Liu AYJJoBC, Heat shock promotes inclusion body formation of mutant huntingtin (mHtt) and alleviates mHtt-induced transcription factor dysfunction, 293, 2018, 15581-15593.
61. Caron NS, Banos R, Yanick C, Aly AE, Byrne LM, Smith ED, Xie Y, Smith SE, Potluri N, Black HFJJoN, Mutant huntingtin is cleared from the brain via active mechanisms in Huntington disease, 41, 2021, 780-796.
62. He W-T, Xue W, Gao Y-G, Hong J-Y, Yue H-W, Jiang L-L, Hu H-YJSr, HSP90 recognizes the N-terminus of huntingtin involved in regulation of huntingtin aggregation by USP19, 7, 2017, 14797.
63. Kim YE, Hosp F, Frottin F, Ge H, Mann M, Hayer-Hartl M, Hartl FUJMc, Soluble oligomers of PolyQ-expanded huntingtin target a multiplicity of key cellular factors, 63, 2016, 951-964.
64. Guo S, Wang H, Yin YJFian, Microglia polarization from M1 to M2 in neurodegenerative diseases, 14, 2022, 815347.
65. Yao K, Zu H-bJI, Microglial polarization: novel therapeutic mechanism against Alzheimer's disease, 28, 2020, 95-110.
66. Song GJ, Suk KJFian, Pharmacological modulation of functional phenotypes of microglia in neurodegenerative diseases, 9, 2017, 139.
67. Du L, Zhang Y, Chen Y, Zhu J, Yang Y, Zhang H-LJMn, Role of microglia in neurological disorders and their potentials as a therapeutic target, 54, 2017, 7567-7584.
68. Takahashi Y, Yu Z, Sakai M, Tomita HJFicn, Linking activation of microglia and peripheral monocytic cells to the pathophysiology of psychiatric disorders, 10, 2016, 144.
69. Palpagama TH, Waldvogel HJ, Faull RL, Kwakowsky AJFimn, The role of microglia and astrocytes in Huntington's disease, 12, 2019, 258.
70. Yang H-M, Yang S, Huang S-S, Tang B-S, Guo J-FJFian, Microglial activation in the pathogenesis of Huntington's disease, 9, 2017, 193.
71. Tanaka M, Vécsei LJAiC, Medicine E, Monitoring the kynurenine system: Concentrations, ratios or what else?, 30, 2021, 775-778.
72. Jimenez-Sanchez M, Licitra F, Underwood BR, Rubinsztein DCJCSHpim, Huntington's disease: mechanisms of pathogenesis and therapeutic strategies, 7, 2017, a024240.
73. Mrštná K, Krčmová LK, Švec FJCCA, Advances in kynurenine analysis, 547, 2023, 117441.
74. Pressey JC, de Saint-Rome M, Raveendran VA, Woodin MAJPR, Chloride transporters controlling neuronal excitability, 103, 2023, 1095-1135.
75. Wang L. Palmitoylation on NMDA receptor trafficking and function in corticostriatal co-culture from HD mouse model. University of British Columbia (2015).
76. Zhao X, Chen X-Q, Han E, Hu Y, Paik P, Ding Z, Overman J, Lau AL, Shahmoradian SH, Chiu WJPotNAoS, TRiC subunits enhance BDNF axonal transport and rescue striatal atrophy in Huntington's disease, 113, 2016, E5655-E5664.
77. Nguyen KQ, Rymar VV, Sadikot AFJFicn, Impaired TrkB signaling underlies reduced BDNF-mediated trophic support of striatal neurons in the R6/2 mouse model of Huntington's disease, 10, 2016, 37.
78. Anglada-Huguet M, Vidal-Sancho L, Cabezas-Llobet N, Alberch J, Xifró XJHsdmp, models c, Pathogenesis of Huntington's disease: how to fight excitotoxicity and transcriptional dysregulation, 2017.

79. Kerkis I, Araldi RP, Wenceslau CV, Mendes TB. Advances in cellular and cell-free therapy medicinal products for Huntington disease treatment. In. From Pathophysiology to Treatment of Huntington's Disease: IntechOpen; 2022.
80. Nakamura T, Lipton SAJA, signaling r, Nitric oxide-dependent protein post-translational modifications impair mitochondrial function and metabolism to contribute to neurodegenerative diseases, 32, 2020, 817-833.
81. Chang R, Liu X, Li S, Li X-JJDd, development, therapy, Transgenic animal models for study of the pathogenesis of Huntington's disease and therapy, 2015, 2179-2188.
82. Ghosh R, Tabrizi SJJHocn, Huntington disease, 147, 2018, 255-278.
83. Tabrizi SJ, Schobel S, Gantman EC, Mansbach A, Borowsky B, Konstantinova P, Mestre TA, Panagoulias J, Ross CA, Zauderer MJTLN, A biological classification of Huntington's disease: the Integrated Staging System, 21, 2022, 632-644.
84. Dayalu P, Albin RLJNc, Huntington disease: pathogenesis and treatment, 33, 2015, 101-114.
85. Blumenstock S, Dudanova IJFin, Cortical and striatal circuits in Huntington's disease, 14, 2020, 82.
86. Matz OC, Spocter M, Spocter MAJC, The effect of Huntington's disease on the basal nuclei: A review, 14, 2022.
87. Righy C, T Bozza M, F Oliveira M, A Bozza FJCN, Molecular, cellular and clinical aspects of intracerebral hemorrhage: are the enemies within?, 14, 2016, 392-402.
88. Aldous SG, Smith EJ, Landles C, Osborne GF, Cañibano-Pico M, Nita IM, Phillips J, Zhang Y, Jin B, Hirst MBJB, A CAG repeat threshold for therapeutics targeting somatic instability in Huntington's disease, 147, 2024, 1784-1798.
89. Mestre TA, van Duijn E, Davis AM, Bachoud-Lévi AC, Busse M, Anderson KE, Ferreira JJ, Mahlknecht P, Tumas V, Sampaio CJMD, Rating scales for behavioral symptoms in Huntington's disease: Critique and recommendations, 31, 2016, 1466-1478.
90. Mestre TA, Busse M, Davis AM, Quinn L, Rodrigues FB, Burgunder JM, Carlozzi NE, Walker F, Ho AK, Sampaio CJMdcp, Rating scales and performance-based measures for assessment of functional ability in Huntington's disease: critique and recommendations, 5, 2018, 361-372.
91. Bennasar M, Hicks Y, Clinch S, Jones P, Holt C, Rosser A, Busse MJIToNS, Engineering R, Automated assessment of movement impairment in Huntington's disease, 26, 2018, 2062-2069.
92. Guo Q, Huang B, Cheng J, Seefelder M, Engler T, Pfeifer G, Oeckl P, Otto M, Moser F, Maurer MJN, The cryo-electron microscopy structure of huntingtin, 555, 2018, 117-120.
93. Kumar A, Kumar V, Singh K, Kumar S, Kim Y-S, Lee Y-M, Kim J-JJBs, Therapeutic advances for Huntington's disease, 10, 2020, 43.
94. Rodrigues FB, Ferreira JJ, Wild EJJJoHsd, Huntington's disease clinical trials corner: June 2019, 8, 2019, 363-371.
95. Tabrizi SJ, Leavitt BR, Landwehrmeyer GB, Wild EJ, Saft C, Barker RA, Blair NF, Craufurd D, Priller J, Rickards HJNEJoM, Targeting huntingtin expression in patients with Huntington's disease, 380, 2019, 2307-2316.
96. Rodrigues FB, Wild EJJJoHsd, Huntington's disease clinical trials corner: February 2018, 7, 2018, 89-98.
97. Wright DJ, Renoir T, Gray LJ, Hannan AJJNDP, Mechanisms,, Targets PT, Huntington's Disease: Pathogenic mechanisms and therapeutic targets, 2017, 93-128.
98. Coppen EM, Roos RAJD, Current pharmacological approaches to reduce chorea in Huntington's disease, 77, 2017, 29-46.
99. Feinstein E, Walker RJCTOiN, An update on the treatment of chorea, 20, 2018, 1-15.
100. Frank S, Testa CM, Stamler D, Kayson E, Davis C, Edmondson MC, Kinel S, Leavitt B, Oakes D, O'Neill CJJ, Effect of deutetrabenazine on chorea among patients with Huntington disease: a randomized clinical trial, 316, 2016, 40-50.
101. Saft C, Burgunder J-M, Dose M, Jung HH, Katzenschlager R, Priller J, Nguyen HP, Reetz K, Reilmann R, Seppi KJNr, practice, Symptomatic treatment options for Huntington's disease (guidelines of the German Neurological Society), 5, 2023, 61.
102. Alharthi MSJM, A narrative review of phase III and IV clinical trials for the pharmacological treatment of Huntington's disease in adults, 103, 2024, e41073.
103. Tan AM, Geva M, Goldberg YP, Schuring H, Sanson B-J, Rosser A, Raymond L, Reilmann R, Hayden MR, Anderson KJJoHsD, Antidopaminergic medications in Huntington's disease, 2025, 18796397241304312.
104. Byrne LM, Wild EJJJoHsd, Cerebrospinal fluid biomarkers for Huntington's disease, 5, 2016, 1-13.
105. Vodičková Kepková K, Vodička PJBfHsDICO, Mitochondrial/Oxidative Stress Biomarkers in Huntington's Disease, 2023, 321-350.
106. Guo S, Yang J, Jiang B, Zhou N, Ding H, Zhou G, Wu S, Suo A, Wu X, Xie WJSR, MicroRNA editing patterns in Huntington's disease, 12, 2022, 3173.
107. Martí-Martínez S, Valor LMJIjoms, A glimpse of molecular biomarkers in Huntington's disease, 23, 2022, 5411.
108. Zeun P, Scahill RI, Tabrizi SJ, Wild EJJM, Neuroscience C, Fluid and imaging biomarkers for Huntington's disease, 97, 2019, 67-80.
109. Fanijo S, Hanson U, Akindahunsi T, Abijo I, Dawotola TBJWJoAR, Reviews, Artificial intelligence-powered analysis of medical images for early detection of neurodegenerative diseases, 19, 2023, 1578-1587.
110. Johnson EB, Gregory SJPimb, science t, Huntington's disease: brain imaging in Huntington's disease, 165, 2019, 321-369.
111. Scahill RI, Andre R, Tabrizi SJ, Aylward EHJHocn, Structural imaging in premanifest and manifest Huntington disease, 144, 2017, 247-261.
112. Farag M, Knights H, Scahill RI, McColgan P, Estevez-Fraga CJMDCP, Neuroimaging Techniques in Huntington's Disease: A Critic Review 2025; 12: 561-576.
113. Scahill RI, Zeun P, Osborne-Crowley K, Johnson EB, Gregory S, Parker C, Lowe J, Nair A, O'Callaghan C, Langley CJTLN, Biological and clinical characteristics of gene carriers far from predicted onset in the Huntington's disease Young Adult Study (HD-YAS): a cross-sectional analysis, 19, 2020, 502-512.
114. Langbehn DR, Stout JC, Gregory S, Mills JA, Durr A, Leavitt BR, Roos RA, Long JD, Owen G, Johnson HJJn, Association of CAG repeats with long-term progression in Huntington disease, 76, 2019, 1375-1385.
115. Corey-Bloom J, Aikin AM, Gutierrez AM, Nadhem JS, Howell TL, Thomas EAJBr, Beneficial effects of glatiramer acetate in Huntington's disease mouse models: Evidence for BDNF-elevating and immunomodulatory mechanisms, 1673, 2017, 102-110.
116. Kasindi A, Fuchs D-T, Koronyo Y, Rentsendorj A, Black KL, Koronyo-Hamaoui MJC, Glatiramer acetate

immunomodulation: evidence of neuroprotection and cognitive preservation, 11, 2022, 1578.
117. Achenbach J, Saft C, Faissner S, Ellrichmann GJTAiND, Positive effect of immunomodulatory therapies on disease progression in Huntington's disease? Data from a real-world cohort, 15, 2022, 17562864221109750.
118. Gibson JS, Claassen DOJEoop, State-of-the-art pharmacological approaches to reduce chorea in Huntington's disease, 22, 2021, 1015-1024.
119. Li Y, Hai S, Zhou Y, Dong BRJCDoSR, Cholinesterase inhibitors for rarer dementias associated with neurological conditions, 2015.
120. Eddy CM, Parkinson EG, Rickards HEJTLP, Changes in mental state and behaviour in Huntington's disease, 3, 2016, 1079-1086.
121. Cankaya S, Cankaya B, Kilic U, Kilic E, Yulug BJDic, The therapeutic role of minocycline in Parkinson's disease, 8, 2019, 212553.
122. Shin JH, Yang H-J, Ahn JH, Jo S, Chung SJ, Lee J-Y, Kim HS, Kim MJJomd, Evidence-based review on symptomatic management of Huntington's disease, 17, 2024, 369.
123. Estévez-Fraga C, Aviles Olmos I, Mananes Barral V, Lopez-Sendon Moreno JLJEOoOD, Therapeutic advances in Huntington's disease, 4, 2016, 809-821.
124. Müller TJEOoID, Investigational agents for the management of Huntington's disease, 26, 2017, 175-185.
125. Kunkanjanawan T, Carter R, Ahn K-S, Yang J, Parnpai R, Chan AWJSDALSR, Induced pluripotent HD monkey stem cells derived neural cells for drug discovery, 22, 2017, 696-705.
126. Makeeva VS, Dyrkheeva NS, Lavrik OI, Zakian SM, Malakhova AAJIJoMS, Mutant-huntingtin molecular pathways elucidate new targets for drug repurposing, 24, 2023, 16798.
127. Yakupova EI, Bobyleva LG, Vikhlyantsev IM, Bobylev AGJBr, Congo Red and amyloids: history and relationship, 39, 2019, BSR20181415.
128. Dapson RWJB, Histochemistry, Amyloid from a histochemical perspective. A review of the structure, properties and types of amyloid, and a proposed staining mechanism for Congo red staining, 93, 2018, 543-556.
129. Berger ZJDATftSoND, Triplet repeat diseases: the role of fly models in understanding disease mechanisms and designing possible therapies, 2020, 183-213.
130. Duarte-Silva S, Silva-Fernandes A, Neves-Carvalho A, Soares-Cunha C, Teixeira-Castro A, Maciel PJN, Combined therapy with m-TOR-dependent and-independent autophagy inducers causes neurotoxicity in a mouse model of Machado–Joseph disease, 313, 2016, 162-173.
131. Tong H, Yang T, Xu S, Li X, Liu L, Zhou G, Yang S, Yin S, Li X-J, Li SJIJoMS, Huntington's disease: complex pathogenesis and therapeutic strategies, 25, 2024, 3845.
132. Thellung S, Corsaro A, Nizzari M, Barbieri F, Florio TJIjoms, Autophagy activator drugs: a new opportunity in neuroprotection from misfolded protein toxicity, 20, 2019, 901.
133. Corey-Bloom J, Jia H, Aikin AM, Thomas EAJJoHsd, Disease modifying potential of glatiramer acetate in Huntington's disease, 3, 2014, 311-316.
134. Quinn N, Marsden CDJJoN, Neurosurgery, Psychiatry, A double blind trial of sulpiride in Huntington's disease and tardive dyskinesia, 47, 1984, 844-847.
135. Chen M, Ona VO, Li M, Ferrante RJ, Fink KB, Zhu S, Bian J, Guo L, Farrell LA, Hersch SMJNm, Minocycline inhibits caspase-1 and caspase-3 expression and delays mortality in a transgenic mouse model of Huntington disease, 6, 2000, 797-801.
136. Heckmann J, Legg P, Sklar D, Fine J, Bryer A, Kies BJN, IV amantadine improves chorea in Huntington's disease: an acute randomized, controlled study, 63, 2004, 597-598.
137. O'Suilleabhain P, Dewey Jr RBJAon, A randomized trial of amantadine in Huntington disease, 60, 2003, 996-998.
138. Lee S-T, Chu K, Park J-E, Kang L, Ko S-Y, Jung K-H, Kim MJBr, Memantine reduces striatal cell death with decreasing calpain level in 3-nitropropionic model of Huntington's disease, 1118, 2006, 199-207.
139. Ravikumar B, Vacher C, Berger Z, Davies JE, Luo S, Oroz LG, Scaravilli F, Easton DF, Duden R, O'Kane CJJNg, Inhibition of mTOR induces autophagy and reduces toxicity of polyglutamine expansions in fly and mouse models of Huntington disease, 36, 2004, 585-595.
140. Bhatia S, Natural polymer drug delivery systems, Springer, 2016.
141. Mustafa G, Hassan D, Zeeshan M, Ruiz-Pulido G, Ebrahimi N, Mobashar A, Pourmadadi M, Rahdar A, Sargazi S, Fathi-karkan SJJoDDS, Technology, Advances in nanotechnology versus stem cell therapy for the theranostics of Huntington's disease, 87, 2023, 104774.
142. Liu X-g, Lu S, Liu D-q, Zhang L, Zhang L-x, Yu X-l, Liu R-tJBr, ScFv-conjugated superparamagnetic iron oxide nanoparticles for MRI-based diagnosis in transgenic mouse models of Parkinson's and Huntington's diseases, 1707, 2019, 141-153.
143. Zhang Y, Yang H, Wei D, Zhang X, Wang J, Wu X, Chang J. Mitochondria-targeted nanoparticles in treatment of neurodegenerative diseases. In. Exploration. Vol 1: Wiley Online Library; 2021:20210115.
144. Rohiwal SS, Klima J, Vaškovičová M, Senigl F, Šlouf M, Pavlova E, Štěpánek P, Stieger K, Ellederova Z. I08 Nanoparticle based CRSIPR/CAS gene editing system to treat huntington's disease. In: BMJ Publishing Group Ltd; 2018.
145. Wenceslau CV, de Souza DM, Mambelli-Lisboa NC, Ynoue LH, Araldi RP, da Silva JM, Pagani E, Haddad MS, Kerkis IJC, Restoration of BDNF, DARPP32, and D2R expression following intravenous infusion of human immature dental pulp stem cells in Huntington's disease 3-NP rat model, 11, 2022, 1664.
146. Li M, Izpisua Belmonte JCJNEJoM, Organoids—preclinical models of human disease, 380, 2019, 569-579.
147. Piao X, Li D, Liu H, Guo Q, Yu YJP, Cell, Advances in gene and cellular therapeutic approaches for Huntington's disease, 16, 2025, 307-337.
148. Pischiutta F, Caruso E, Cavaleiro H, Salgado AJ, Loane DJ, Zanier ERJEn, Mesenchymal stromal cell secretome for traumatic brain injury: Focus on immunomodulatory action, 357, 2022, 114199.
149. Nedosekin DA, Chen T, Ayyadevara S, Zharov VP, Shmookler Reis RJJSR, Label-free photothermal disruption of cytotoxic aggregates rescues pathology in a C. elegans model of Huntington's disease, 11, 2021, 19732.
150. Lum PT, Sekar M, Gan SH, Bonam SR, Shaikh MFJAcn, Protective effect of natural products against Huntington's disease: An overview of scientific evidence and understanding their mechanism of action, 12, 2021, 391-418.
151. Cong W, Bai R, Li Y-F, Wang L, Chen CJAam, interfaces, Selenium nanoparticles as an efficient nanomedicine for the therapy of Huntington's disease, 11, 2019, 34725-34735.

152. Birolini G, Valenza M, Ottonelli I, Passoni A, Favagrossa M, Duskey JT, Bombaci M, Vandelli MA, Colombo L, Bagnati RJJoCR, Insights into kinetics, release, and behavioral effects of brain-targeted hybrid nanoparticles for cholesterol delivery in Huntington's disease, 330, 2021, 587-598.
153. Birolini G, Valenza M, Ottonelli I, Talpo F, Minoli L, Cappelleri A, Bombaci M, Caccia C, Leoni V, Passoni A, Cholesterol-laden brain-permeable nanoparticles support long-lasting cognitive recovery and motor amelioration in the slow-progressing zQ175DN mouse model of Huntington's Disease, 2022.
154. Sava V, Fihurka O, Khvorova A, Sanchez-Ramos JJNN, Biology, Medicine, Enriched chitosan nanoparticles loaded with siRNA are effective in lowering Huntington's disease gene expression following intranasal administration, 24, 2020, 102119.
155. Bhatt R, Singh D, Prakash A, Mishra NJDd, Development, characterization and nasal delivery of rosmarinic acid-loaded solid lipid nanoparticles for the effective management of Huntington's disease, 22, 2015, 931-939.
156. Xing Y, Meng B, Chen QJIJoMS, Cyclodextrin-Containing Drug Delivery Systems and Their Applications in Neurodegenerative Disorders, 25, 2024, 10834.
157. Escalona-Rayo O, Fuentes-Vazquez P, Leyva-Gomez G, Cisneros B, Villalobos R, Magana JJ, Quintanar-Guerrero DJDD, Pharmacy I, Nanoparticulate strategies for the treatment of polyglutamine diseases by halting the protein aggregation process, 43, 2017, 871-888.
158. Malhotra M, Gooding M, Evans JC, O'Driscoll D, Darcy R, O'Driscoll CMJEJoPS, Cyclodextrin-siRNA conjugates as versatile gene silencing agents, 114, 2018, 30-37.
159. Debnath K, Pradhan N, Singh BK, Jana NR, Jana NRJAam, interfaces, Poly (trehalose) nanoparticles prevent amyloid aggregation and suppress polyglutamine aggregation in a Huntington's disease model mouse, 9, 2017, 24126-24139.
160. Sandhir R, Yadav A, Mehrotra A, Sunkaria A, Singh A, Sharma SJNm, Curcumin nanoparticles attenuate neurochemical and neurobehavioral deficits in experimental model of Huntington's disease, 16, 2014, 106-118.
161. Labanca F, Ullah H, Khan H, Milella L, Xiao J, Dajic-Stevanovic Z, Jeandet PJCN, Therapeutic and mechanistic effects of curcumin in Huntington's disease, 19, 2021, 1007-1018.
162. Lata JMG. The Role of Nanotechnology to Overcome the Natural Compounds Limitations in the Treatment of Alzheimer's and Huntington's Diseases. Universidade do Porto (Portugal) (2020).
163. Yavarpour-Bali H, Ghasemi-Kasman M, Pirzadeh MJIjon, Curcumin-loaded nanoparticles: A novel therapeutic strategy in treatment of central nervous system disorders, 2019, 4449-4460.
164. Singh S, Hema, Sharma N, Sachdeva M, Behl T, Zahoor I, Fuloria NK, Sekar M, Fuloria S, Subramaniyan VJES, Research P, Focusing the pivotal role of nanotechnology in Huntington's disease: an insight into the recent advancements, 29, 2022, 73809-73827.
165. Ramachandran S, Thangarajan SJC-BI, A novel therapeutic application of solid lipid nanoparticles encapsulated thymoquinone (TQ-SLNs) on 3-nitroproponic acid induced Huntington's disease-like symptoms in wistar rats, 256, 2016, 25-36.
166. Ramachandran S, Thangarajan SJMBD, Thymoquinone loaded solid lipid nanoparticles counteracts 3-Nitropropionic acid induced motor impairments and neuroinflammation in rat model of Huntington's disease, 33, 2018, 1459-1470.
167. Ramachandran S, Thangarajan SJN, Thymoquinone-loaded solid lipid nanoparticles mitigate 3-Nitropropionic acid-induced mitochondrial dysfunction and oxidative damage via regulating PGC-1α/Nrf2 pathway, 108, 2025, 191-205.
168. Akila R, SHAJI DMJIJPPS, Ginger Loaded Chitosan Nanoparticles for The Management of 3–Nitropropionic Acid-Induced Huntington's Disease-like Symptoms In Male Wistar Rats, 14, 2021, 28-36.
169. Joshi AS, Singh V, Gahane A, Thakur AKJACN, Biodegradable nanoparticles containing mechanism based peptide inhibitors reduce polyglutamine aggregation in cell models and alleviate motor symptoms in a Drosophila model of Huntington's disease, 10, 2018, 1603-1614.
170. Godinho BM, Ogier JR, Darcy R, O'Driscoll CM, Cryan JFJMp, Self-assembling modified β-cyclodextrin nanoparticles as neuronal siRNA delivery vectors: Focus on Huntington's disease, 10, 2013, 640-649.
171. Ganesh S, Chithambaram T, Krishnan NR, Vincent DR, Kaliappan J, Srinivasan KJD, Exploring huntington's disease diagnosis via artificial intelligence models: a comprehensive review, 13, 2023, 3592.
172. André EM, Passirani C, Seijo B, Sanchez A, Montero-Menei CNJB, Nano and microcarriers to improve stem cell behaviour for neuroregenerative medicine strategies: Application to Huntington's disease, 83, 2016, 347-362.
173. Fatima J, Siddique YHJC, Targets-CNS ND-D, Disorders) N, Application of Nanocomposites and Nanoparticles in Treating Neurodegenerative Disorders, 23, 2024, 1217-1233.
174. Guo Z-H, Khattak S, Rauf MA, Ansari MA, Alomary MN, Razak S, Yang C-Y, Wu D-D, Ji X-YJM, Role of nanomedicine-based therapeutics in the treatment of CNS disorders, 28, 2023, 1283.
175. Ananbeh H, Vodicka P, Kupcova Skalnikova HJIjoms, Emerging roles of exosomes in Huntington's disease, 22, 2021, 4085.
176. Kim A, Lalonde K, Truesdell A, Gomes Welter P, Brocardo PS, Rosenstock TR, Gil-Mohapel JJIjoms, New avenues for the treatment of Huntington's disease, 22, 2021, 8363.

How to cite this article:
Neethu MV, Sharma S, Narwal N, Kumari S and Anjumol VM: Nanomedicine for huntington's disease: a review of current strategies, challenges, and future directions. Int J Pharm Sci & Res 2026; 17(1): 75-90. doi: 10.13040/IJPSR.0975-8232.17(1).75-90.