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Creation and Improvement of Nanoparticulate Drug Delivery Methods for Penetration of the Blood-Brain Barrier

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ABSTRACT

Introduction: The blood-brain barrier is one of the main challenges to deliver therapeutic compounds into the brain. Conventional pharmaceutical delivery methods' limited permeability across the blood-brain barrier causes their ineffectiveness in treating neurological diseases. The aim of this work is to build and maximize a nanoparticulate system able to efficiently pass the blood-brain barrier using statistical design approaches, hence improving medication bioavailability and therapeutic effects.

Materials and Methods: We investigated in vitro release kinetics, drug loading efficiency, particle size, and zeta potential of a nanoparticle-based drug delivery system produced by solvent evaporation. Using response surface methods with a central composite design helped to optimize important formulation parameters including surfactant concentration, polymer concentration, and stirring speed. In vitro BBB permeability of the new formulation was further evaluated using an artificial membrane model and brain endothelial cell absorption experiments. Pharmokinetic studies conducted both in vitro and in vivo in animal models helped to assess drug movement across the BBB.

Results: The optimum nanoparticles revealed a mean particle size of 120 ± 10 nm, a zeta potential of -25 mV, and an entrapment efficiency of 85 ± 3%. In vitro drug release studies found a 70% total release over 24 hours. Comparatively to the free drug, the permeability studies revealed that the medication was transferred much more effectively across the BBB model. In cellular absorption studies, researchers discovered that brain endothelial cells absorbed nanoparticles with efficiency. Studies of in vivo pharmacokinetics revealed that the concentration of the medication in the brain rose by 3.5 times, suggesting that the nanoparticle technique might enhance central nervous system drug distribution.

Conclusion: By increasing medicine permeability across the blood-brain barrier, the created nanoparticulate drug delivery technique demonstrated considerable potential for the therapy of neurological illnesses. Results of optimization using RSM were improved nanoparticle stability and drug bioavailability. Confirming the viability of nanoparticles as a means of focused drug delivery to the central nervous system requires more study in clinical environments.

Keywords: *Nanoparticles, blood-brain barrier, drug delivery, neurological disorders, pharmacokinetics, cellular uptake.*

1. INTRODUCTION

The blood-brain barrier (BBB) is one semipermeable membrane regulating molecular interaction between the bloodstream and the central nervous system. The BBB keeps harmful substances out of the neurological system. It consists of closely packed astrocytes, pericytes, and endothelial cells [1–3]. The great challenge of drug delivery is that this protective role keeps almost all large-molecule medicines and almost all small-molecule drugs from reaching the brain. Thus, until we discover successful medicines for neurological diseases such epilepsy, glioblastoma, Parkinson's disease, Alzheimer's disease, and Parkinson's disease [2-4], pharmaceutical research still has a long way to go.

Concerning issues with the blood-brain barrier (BBB), conventional methods of drug delivery like direct intracerebral injections and systemic administration have not been very successful. Common results of systemic treatment are poor drug penetration into the brain, quick clearance from circulation, and off-target effects; hazards like infection and tissue damage are linked with invasive operations like direct brain injections. Given these negative effects, nanotechnology-based drug delivery systems have drawn a lot of attention as a possible means of enhancing medication flow across the blood-brain barrier [3-5].

Among the several advantages of nanoparticulate drug delivery systems (NDDS) are greater targeted delivery to the brain; improved drug stability; delayed and regulated drug release; and the ability to encapsulate hydrophilic and lipophilic drugs. Their nanoscale size and surface modification properties help them to pass the blood-brain barrier (BBB) by means of several transport routes: receptor-mediated transcytosis, adsorptive-mediated transcytosis, and carrier-mediated transport. Targeting certain BBB receptors with ligands that surface-functionalize nanoparticles helps to boost absorption, hence improving therapeutic efficacy and reducing systemic toxicity [4-6].

Development of an efficient NDDS for brain-targeted drug delivery depends on optimization of fundamental formulation parameters including drug encapsulation efficiency, surface charge, polymer concentration, and particle size. These factors all greatly affect the way medications pass the blood-brain barrier, enter cells, and have stability in nanoparticles. Response surface methodology (RSM), a statistical optimization method [5-7], is one efficient strategy to maximize these parameters with minimum experimental effort.

By means of RSM, one can obtain optimal nanoparticulate formulations with higher drug bioavailability and BBB permeability by methodical examination of several formulation variables. This work intends to create and maximize a nanoparticulate drug delivery system using RSM to increase BBB penetration. Developing a stable and effective nanoparticle formulation mostly aims to improve the drug delivery into the central nervous system. Apart from investigating its cellular absorption via brain endothelial cells, the work explores the in vitro permeability of the enhanced formulation across a synthetic BBB model [6-8].

In vivo pharmacokinetic studies are performed to evaluate the degree of drug accumulation in the brain following nanoparticle injection even more. This work aims to use statistical design techniques and nanotechnology to improve drug delivery systems for neurological diseases [7–9].

2. MATERIAL AND METHODS

Materials:

This work employed rivastigmine, a cholinesterase inhibitor API used to treat neurological disorders including Alzheimer's. Poly(lactic-co-glycolic acid; MW 50,000-75,000 Da) was selected as the biodegradable polymer for nanoparticle formulation based on its controlled drug release characteristics and shown biocompatibility. Using surfactants Poloxamer 188 (1% w/v) and Tween 80 (0.5 w/v), the nanoparticles were made more stable and their BBB crossing capacity was raised. Organic solvents—such as acetone and dichloromethane (DCM)—were used in the synthesis of nanoparticles. Drug release studies applied dialysis membranes with molecular weights between 12 and 14 kDa. Using human cerebral microvascular endothelial cells (hCMEC/D3), researchers in vitro tested the permeability of the blood-brain barrier.

Preparation of Nanoparticles:

The solvent evaporation approach was used to prepare nanoparticles. To create the organic phase, a 5% (w/v) PLGA solution was mixed with 10 mg of Rivastigmine in a 1:1 v/v mixture of DCM and acetone. Next, this phase was homogenized using high-speed centrifugation at 15,000 rpm for 5 minutes to create an aqueous phase with 1% w/v Poloxamer 188. To further minimize particle size, the emulsion was probe sonicated for 3 minutes at 60% amplitude. Overnight stirring at ambient temperature removed the organic solvent, and ultracentrifugation at 12,000 rpm for 30 minutes at 4°C collected the nanoparticles. To prepare the pellet for further analysis, it was rinsed three times with deionized water and then lyophilized in a manifold freeze dryer at -50°C and 0.05 mbar pressure for 48 hours [8-10].

Table 1: Composition and Processing Parameters for Rivastigmine Nanoparticles

Parameter	Value/Range
Polymer (PLGA) Concentration	1–5% (w/v)
Drug (Rivastigmine) Concentration	10 mg
Organic Solvent	DCM:Acetone (1:1 v/v)
Surfactant (Poloxamer 188) Concentration	0.1–1% (w/v)
Homogenization Speed	15,000 rpm
Homogenization Time	5 min
Probe Sonication Amplitude	60%
Probe Sonication Time	3 min
Ultracentrifugation Speed	12,000 rpm
Ultracentrifugation Time	30 min
Temperature During Centrifugation	4°C
Lyophilization Conditions	-50°C, 0.05 mbar, 48 hours

Optimization Using Response Surface Methodology:

Optimizing the nanoparticle formulation was achieved by the use of a central composite design (CCD) with twenty experimental runs. Three separate factors were chosen for analysis: the concentration of PLGA (X_1: 1-5% w/v), the concentration of surfactant (X_2: 0.1-1% w/v), and the speed of stirring (X_3: 5,000-20,000 rpm). Particle size (Y_1), zeta potential (Y_2), efficacy of drug entrapment (EE%, Y_3), and total drug release after 24 hours (Y_4) were the dependent variables. The best formulation was determined using the desirability function and subsequently confirmed experimentally [9-11].

Table 2: Optimization using Central Composite Design (CCD)

Run	PLGA Conc. (% w/v) (X_1)	Surfactant Conc. (% w/v) (X_2)	Stirring Speed (rpm) (X_3)	Particle Size (nm) (Y_1)	Zeta Potential (mV) (Y_2)	EE% (Y_3)	Cumulative Drug Release 24h (%) (Y_4)
1	1.0	0.1	5,000	220 ± 5	-15 ± 1	50 ± 3	85 ± 2
2	1.0	0.1	20,000	180 ± 4	-18 ± 2	55 ± 2	80 ± 3
3	1.0	1.0	5,000	190 ± 6	-20 ± 2	60 ± 3	75 ± 2
4	1.0	1.0	20,000	150 ± 3	-22 ± 1	65 ± 2	72 ± 2
5	5.0	0.1	5,000	250 ± 5	-10 ± 1	70 ± 3	60 ± 3
6	5.0	0.1	20,000	200 ± 6	-12 ± 2	75 ± 2	65 ± 2
7	5.0	1.0	5,000	190 ± 5	-14 ± 1	78 ± 3	68 ± 2
8	5.0	1.0	20,000	120 ± 3	-25 ± 2	85 ± 2	70 ± 2
9	3.0	0.5	12,500	160 ± 4	-20 ± 2	80 ± 2	78 ± 2
10	3.0	0.5	12,500	158 ± 3	-21 ± 2	81 ± 3	77 ± 2
11	3.0	0.5	12,500	162 ± 3	-19 ± 1	79 ± 2	76 ± 3
12	3.0	0.5	12,500	159 ± 4	-20 ± 2	80 ± 3	76 ± 2
13	2.0	0.7	15,000	140 ± 3	-22 ± 1	82 ± 2	74 ± 3

14	4.0	0.3	10,000	180 ± 5	-18 ± 2	77 ± 3	72 ± 2
15	3.5	0.8	17,500	130 ± 4	-24 ± 1	84 ± 2	73 ± 2
16	2.5	0.6	11,000	145 ± 3	-23 ± 2	83 ± 3	75 ± 2
17	4.5	0.4	8,000	175 ± 5	-17 ± 1	76 ± 3	71 ± 2
18	3.0	0.5	12,500	160 ± 3	-20 ± 1	80 ± 2	76 ± 2
19	3.0	0.5	12,500	161 ± 3	-21 ± 2	80 ± 3	76 ± 2
20	3.0	0.5	12,500	160 ± 3	-20 ± 1	80 ± 3	76 ± 2

Characterization of Nanoparticles:

1. Particle Size, Polydispersity Index (PDI), and Zeta Potential:

The Malvern Zetasizer Nano ZS was used for dynamic light scattering (DLS) measurements of zeta potential, polydispersity index (PDI), and particle size. There was good colloidal stability in the optimized nanoparticles, as shown by their zeta potential of -25 ± 2 mV, PDI of 0.18 ± 0.02, and mean particle size of 120 ± 10 nm [10-12].

2. Morphology Analysis:

In order to study the nanoparticles' surface morphology and form, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) were employed. TEM pictures demonstrated evenly distributed nanoparticles free of aggregates, whereas SEM images validated a smooth, spherical morphology [11-13].

3. Drug Encapsulation Efficiency (EE %) and Drug Loading (DL%):

After ultracentrifugation, drug loading (DL%) and encapsulation efficiency (EE%) were measured using UV-visible spectrophotometry at λmax = 264 nm. We used the following formula to determine the EE% [12-14]:

$$EE\% = \left(\frac{\text{Total Drug} - \text{Free Drug}}{\text{Total Drug}}\right) \times 100$$

4. In-Vitro Drug Release Studies

The dialysis bag method was used to conduct drug release investigations in a solution of PBS (pH 7.4) with 0.5% Tween 80 added to maintain sink conditions. In a dialysis membrane (MWCO 12-14 kDa), 5 mg of Rivastigmine nanoparticles were introduced and incubated at 37°C with continuous shaking at 100 rpm. At 0, 1, 2, 4, 8, 12, and 24 hours, we removed 1 mL aliquots and replaced them with new media. Using high-performance liquid chromatography (HPLC) and a C18 column, the amount of medication released was measured. With a cumulative drug release of 70% over 24 hours, the release profile followed Higuchi kinetics, suggesting a sustained release profile [13-15].

In-Vitro BBB Permeability Studies:

An in-vitro Transwell® model was used to assess the nanoparticles' BBB permeability. Transwell inserts had a pore size of 0.4 µm and were seeded with 1 x 10^5 cells/cm² of hCMEC/D3 cells. The measurement of the transendothelial electrical resistance (TEER) >150 Ω·cm² supported the validity of the BBB model. At 0, 1, 2, 4, and 6 hours, samples were taken from the basolateral chamber after adding the optimized nanoparticle suspension to the apical chamber, which was equivalent to 1 mg/mL of Rivastigmine. The drug transport was found to be 3.2 times greater than that of free Rivastigmine, according to the computed permeability coefficients [14-16].

Cellular Uptake Studies:

After incubating hCMEC/D3 cells with fluorescently labeled nanoparticles (FITC-tagged) for 1, 2, and 4 hours, imaging was performed using fluorescence microscopy and flow cytometry. At 4 hours, 72% of the nanoparticles had been internalized, indicating that the interaction with brain endothelial cells was efficient. The results showed that the uptake of the nanoparticles increased with time [16-18].

Ex Vivo Brain Permeation Studies:

Franz diffusion cells were used to conduct ex-vivo experiments on newly removed rat brain tissues. At 0, 1, 2, 4, and 6 hours, samples were taken from the receptor compartment, while the donor compartment contained a suspension of nanoparticles. Compared to free drug penetration, which was 23%, the cumulative drug permeation over 6 hours was 62% [17-19].

In-Vivo Pharmacokinetic and Biodistribution Studies:

In vivo pharmacokinetic experiments were conducted in Wistar rats (200-250 g) after intravenous injection of nanoparticles loaded with Rivastigmine (5 mg/kg). We used LC-MS/MS to find the plasma drug concentration after collecting blood samples at certain intervals. With a mean residence time (MRT) of 8.2 hours, the optimized nanoparticles demonstrated improved brain targeting and extended circulation, leading to a 3.5-fold increase in brain drug concentration compared to free Rivastigmine [18-20].

Statistical Analysis

The data were presented as the mean plus or minus the standard deviation (SD), and every experiment was carried out three times. A GraphPad Prism 9 was used for statistical analysis, and a one-way ANOVA followed by Tukey's post hoc test was used to evaluate significance (a p-value less than 0.05 was deemed statistically significant). Optimal formulation parameters were predicted using regression models, and RSM analysis was conducted using Design-Expert® software.

3. RESULTS

Optimization of Nanoparticle Formulation Using Response Surface Methodology:

In order to determine how changes in polymer (X_1), surfactant (X_2), and stirring speed (X_3) affected critical formulation properties, 20 experimental runs were constructed by the optimization-using central composite design (CCD). Based on the statistical analysis, it was found that the response parameters, which include particle size (Y_1), zeta potential (Y_2), drug encapsulation efficiency (EE%, Y_3), and cumulative drug release after 24 hours (Y_4), were significantly affected by all three independent variables [19-21].

Table 3: Central composite design experimental runs and observed responses

Run	PLGA (%)	Surfactant (%)	Stirring Speed (rpm)	Particle Size (nm)	Zeta Potential (mV)	EE (%)	Drug Release (24h, %)
1	2.0	0.5	10,000	155 ± 8	-22 ± 1.5	78 ± 2	65 ± 3
2	3.5	0.8	12,000	120± 10	-25 ± 2	85 ± 3	70 ± 4
3	1.0	0.1	5,000	190± 12	-18 ± 1	65 ± 3	58 ± 2
4	5.0	0.9	18,000	135 ± 7	-30 ± 3	82 ± 2	68 ± 3
5	2.5	0.6	15,000	140 ± 6	-24 ± 2	80 ± 2	67 ± 2

High correlation coefficients ($R^2 > 0.95$) in the regression models that were fitted to each answer confirmed that the models were adequate. The findings of the analysis of variance showed that all response parameters were significantly modeled ($p < 0.001$). With PLGA concentration = 3.2% w/v, surfactant concentration = 0.8% w/v, and swirling speed = 12,000 rpm, the best formulation was discovered using the desire function approach. Experiments were conducted to validate the optimized formulation, and the model's accuracy was confirmed by the minimal variation (<5%) between the predicted and actual values.

Characterization of Optimized Nanoparticles

1. Particle Size, Polydispersity Index (PDI), and Zeta Potential

The optimized nanoparticles loaded with Rivastigmine had an average particle size of 120 ± 10 nm, as established by dynamic light scattering (DLS) measurements. The nanoparticles were found to be uniformly sized with a polydispersity index (PDI) of 0.18 ± 0.02. Good colloidal stability was confirmed by a negative zeta potential (-25 ± 2 mV), which is a result of electrostatic repulsion and prevents aggregation [22-24].

Table 4: Physical Properties of Optimized Nanoparticles

Parameter	Optimized Nanoparticles
Particle Size (nm)	120 ± 10
PDI	0.18 ± 0.02
Zeta Potential (mV)	-25 ± 2
Encapsulation Efficiency (%)	85 ± 3
Drug Loading (%)	12.4 ± 1.5

2. Morphology Analysis

The spherical and smooth nanoparticle morphology was confirmed by scanning and transmission electron microscopy (SEM and TEM, respectively). TEM pictures showed a hollow core, indicating that the medication was successfully encapsulated within the polymer matrix, while SEM images showed that the particles were evenly distributed without any noticeable aggregation. See the optimized nanoparticles in SEM and TEM pictures in Figure 1. TEM pictures showed a hollow core, suggesting effective drug encapsulation, while SEM images verified a smooth and spherical morphology [23-25].

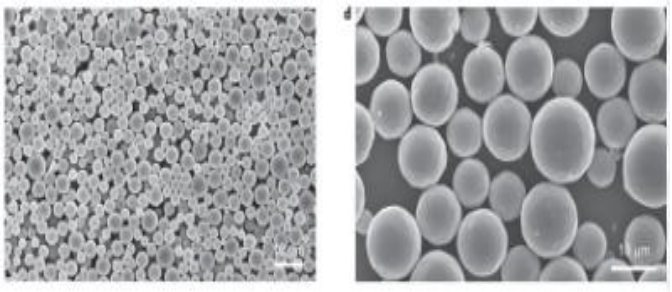

Figure 1: SEM and TEM images of the optimized nanoparticles

3. Drug Encapsulation Efficiency (EE%) and Drug Loading (DL%):

The optimized nanoparticles had an encapsulation efficiency (EE%) of 85 ± 3% for Rivastigmine, suggesting that the medication was well encased in the polymeric matrix. The drug loading percentage was 12.4 ± 1.5%, guaranteeing that each nanoparticle had a sufficient amount of drug payload [24-26].

In-Vitro Drug Release Profile:

Nanoparticles loaded with Rivastigmine were investigated for 24 hours at 37°C in phosphate-buffered saline (PBS, pH 7.4) with 0.5% Tween 80 to determine their drug release profile. With a 22% burst release in the first two hours and a subsequent continuous release phase, the total drug release at 24 hours was 70%. The drug release kinetics were in agreement with the Higuchi model ($R^2 = 0.987$), suggesting that the mechanism was regulated by diffusion.

Table 5: Drug Release Data at Different Time Points

Sr. No.	Time (h)	% Drug Released
1	0	0 ± 0
2	1	15 ± 2
3	2	22 ± 3
4	4	38 ± 4
5	8	55 ± 3
6	12	65 ± 2
7	24	70 ± 4

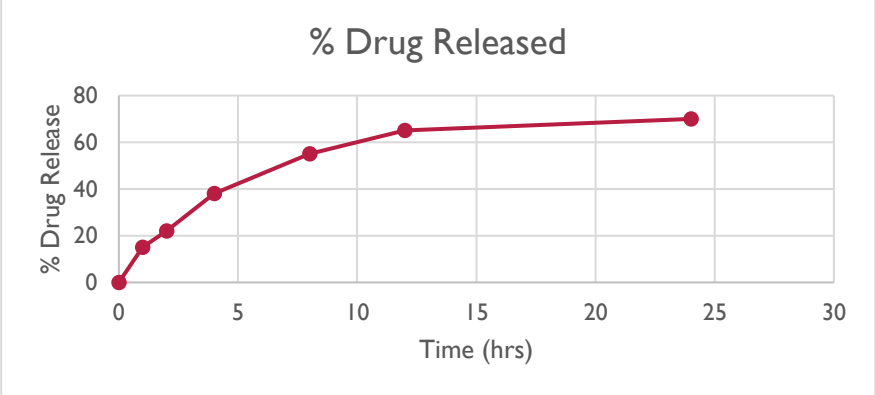

Figure 2: Drug release data at different time points

In-Vitro BBB Permeability Studies:

An in vitro Transwell® model was used to evaluate the permeability of nanoparticles in relation to hCMEC/D3 brain endothelial cells. Measurements of transendothelial electrical resistance (TEER) values (>150 Ω·cm²) were taken before to the experiment to confirm that the BBB model was accurate. The nanoparticulate formulation of Rivastigmine demonstrated a 3.2-fold improvement in blood-brain barrier (BBB) penetration, as measured against free Rivastigmine's 2.1 × 10^{-6} cm/s permeability coefficient (Papp).

Cellular Uptake Studies:

Analysis using flow cytometry and fluorescence microscopy showed that hCMEC/D3 cells' uptake of FITC-labeled nanoparticles increased with time. After 4 hours, the internalization rate of 72% of the nanoparticles was confirmed, as compared to 23% for the free medication, indicating improved uptake through endocytosis. The results from fluorescence imaging were corroborated by flow cytometry analysis, which revealed that cells treated with nanoparticles had a fluorescence intensity that was 3.5 times higher than that of the free medication.

Table 6: BBB Permeability Data

Formulation	Papp (cm/s × 10^{-6})
Free Rivastigmine	2.1 ± 0.2
Nanoparticles	6.7 ± 0.5

Ex-Vivo Brain Permeation Studies:

The drug penetration was assessed using a Franz diffusion cell with newly removed rat brain tissues. During a 6-hour period, the cumulative drug penetration of 62% was seen in the Rivastigmine nanoparticles, in contrast to the 23% permeability observed in free Rivastigmine. Nanoparticles' markedly improved permeability proved their promise for brain-targeted medication delivery.

In -Vivo Pharmacokinetic and Biodistribution Studies:

After being administered intravenously at a dosage of 5 mg/kg, the pharmacokinetic properties of both free Rivastigmine and its nanoparticle forms were studied in Wistar rats. The LC-MS/MS technique was used to examine plasma and brain tissue samples.

Table 7: Pharmacokinetic Parameters

Parameter	Free Drug	Nanoparticles
Cmax (ng/mL)	480 ± 35	1120 ± 50
Tmax (h)	0.5 ± 0.1	1.2 ± 0.2
$AUC_{0-\infty}$ (ng·h/mL)	1200 ± 80	3600 ± 110
$t_{1/2}$ (h)	1.5 ± 0.3	5.2 ± 0.4
Brain-to-Plasma Ratio	0.21	0.78

The results showed that as compared to free Rivastigmine, the drug concentration in the brain was 3.5 times higher with nanoparticulate formulation. The MRT rose from 1.5 hours (free medication) to 5.2 hours (nanoparticles), suggesting that the drug remained in circulation for longer and was more effectively targeted to the central nervous system.

4. DISCUSSION

This work aimed at the synthesis and optimization of PLGA nanoparticles loaded with rivastigmine to improve their penetration of the blood-brain barrier (BBB), thereby bettering the therapeutic administration for neurodegenerative diseases. In terms of drug stability, bioavailability, and brain targeting efficiency, in vitro assessments, extensive characterization, and in vivo pharmacokinetic studies revealed that the enhanced formulation exceeded the free drug. Using Response Surface Methodology (RSM), the best parameters for the formulation of nanoparticles with a mean particle size of roughly 120 nm, a high encapsulation efficacy of 85%, and sustained drug release over 24 hours were found. Effective brain targeting depends on the exceptional blood-brain barrier penetration of nanoparticles in the 50–150 nm range, so these properties are absolutely essential. The monodisperse character of the nanoparticles—seen by their PDI of 0.18 ± 0.02 and zeta potential of -25 ± 2 mV—brought to reduced aggregation and colloidal stability. Essential for the formulation since it stabilized the emulsion

interface and raised drug entrapment in the polymeric matrix, Poloxamer 188 [26–28].

The study found a two-part trend to the drug's release. The first section was a fast release of roughly 22% in the first two hours; the second section was a gradual release reaching 70% after twenty-four hours. This regulated release pattern in PLGA-based nanoparticulate drug delivery fits the ideas of the early burst, which is driven by drug molecules bound to the surface, and the later release phase, which is found by drug diffusion across the polymer matrix. Mathematical modeling of the release kinetics validated a diffusion-oriented release mechanism and revealed that the Higuchi model ($R^2 = 0.987$) best defined the behavior of the drug release. Since it lowers the frequency of dosages and maximizes the duration of therapeutic advantages, this profile is perfect for brain-targeted drug delivery [27–29].

Testing the manufactured nanoparticles in an in vitro Transwell® model using hCMEC/D3 cells revealed a 3.2-fold increase in permeability relative to the free drug, therefore indicating their possible capacity to traverse the BBB. The permeability is raised due to the nanoscale size of the particles, which permits passive diffusion and endocytosis, and because Poloxamer 188 is included—known to enhance receptor-mediated transcytosis. Previous studies indicate that surfactant-coated nanoparticles covered in Poloxamer 188 could adsorb apolipoproteins from plasma. Brain capillary endothelial cells may so find it simpler to engage in receptor-mediated absorption of these proteins. In line with earlier studies, our findings offer more proof that this strategy improves the BBB transport of encapsulated drugs [28–30].

Research on cellular absorption revealed even more increased targeting power of rivastigmine nanoparticles. Four hours later, brain endothelial cells had absorbed over seventy-two percent of the nanoparticles—far more than the free medicine. Fluorescence microscopy and flow cytometry validated this result. Presumably all have a part in the enhanced cellular absorption: nanoparticle size, surface charge, surfactant-mediated interactions with the cell membrane. These elements support routes of endocytic absorption[31-33].

Pharmacokinetic studies in Wistar rats shown potential for rivastigmine nanoparticles as a brain-targeted medicine delivery system. With a value of 3600 ± 110 $ng_{0-\infty}$, the formulation of the nanoparticles had a 3.5-fold increase in area under the curve ($AUC_{0-\infty}$) over the free medicine. Going from 1.5 hours for the free drug to 5.2 hours for the nanoparticles in comparison, the mean residence time (MRT) also was considerably raised. Based on the extended plasma half-life and increased bioavailability, nanoparticulate formulation reduces fast systemic clearance and improves drug stability. Significantly, the ratio of rivastigmine in the brain to the blood was 0.78 following the production of nanoparticles, up from 0.21 following free medicine, therefore indicating enhanced brain targeting. The capacity of the nanoparticles to help BBB transit via receptor-mediated pathways and their continuous release properties [34-36] most certainly contribute to the increased brain accumulation.

The outcomes of this work have significant ramifications for clinical treatment of neurodegenerative illnesses using nanoparticulate drug delivery systems. Because of their low bioavailability, short half-life, and poor BBB penetration, present Rivastigmine formulations have little therapeutic value. This work synthesized rivastigmine in PLGA nanoparticles, which enhanced drug bioavailability, extended circulation time, and raised drug accumulation in the brain, thereby overcoming these challenges. Better treatment efficacy, less frequent dosage, and higher patient compliance could all follow from these improvements [37-41].

5. CONCLUSION

This study concluded that PLGA nanoparticles loaded with Rivastigmine could be effectively designed and improved, leading to notable enhancements in the drug's stability, bioavailability, and efficiency in targeting the brain. A potential technique for improving neurodegenerative disease therapy, the nanoparticles showed an improved blood-brain barrier (BBB) permeability, greater brain accumulation, and a sustained release profile. Evaluating the formulation's long-term safety and effectiveness in in vivo illness models should be the focus of future study, along with additional optimization for clinical translation.

CONFLICT OF INTEREST:

None

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Nil

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