

Formulation and In Vitro Evaluation of Intranasal Medicated Gel for Enhanced Delivery in Alzheimer's Disease

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Abstract:

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory impairment, and neuronal loss. Conventional oral therapies often exhibit limited therapeutic efficacy due to poor blood–brain barrier permeability, extensive first-pass metabolism, and systemic adverse effects. Intranasal drug delivery has emerged as a promising non-invasive approach for direct nose-to-brain transport, enabling rapid drug absorption and enhanced bioavailability in the central nervous system. The present study aimed to formulate and evaluate an intranasal medicated gel for improved drug delivery in the management of Alzheimer's disease. The gel formulations were prepared using suitable mucoadhesive polymers and evaluated for physicochemical properties including appearance, pH, viscosity, gel strength, drug content uniformity, spreadability, and mucoadhesive strength. In vitro drug release studies were performed using diffusion techniques to assess the release behavior of the incorporated drug. The developed formulations exhibited satisfactory physicochemical characteristics, acceptable nasal compatibility, and sustained drug release profiles. Enhanced mucoadhesion and prolonged nasal residence time were observed, indicating the potential of the gel system to improve drug absorption through the nasal mucosa. The findings suggest that the formulated intranasal medicated gel may serve as an effective and patient-friendly platform for targeted brain delivery, offering a promising therapeutic strategy for the treatment of Alzheimer's disease. Further in vivo investigations are warranted to confirm its brain-targeting efficiency and therapeutic effectiveness.

Keywords: Intranasal delivery, Medicated gel, Mucoadhesive polymers, In vitro evaluation, Brain targeting.

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Introduction:

Alzheimer disease (AD) is a progressive neurodegenerative disorder characterized by gradual impairment of memory, cognition, language, and executive functioning [1]. It is the most common cause of dementia worldwide and represents a major public health challenge due to increasing life expectancy and population aging. According to the World Health Organization, dementia affects more than 55 million people globally, with Alzheimer disease accounting for approximately 60–70% of all dementia cases [2]. The prevalence of AD is expected to increase substantially over the coming decades, imposing enormous social, economic, and healthcare burdens on patients, caregivers, and healthcare systems. The pathological hallmarks of Alzheimer disease include extracellular deposition of β -amyloid ($A\beta$) plaques, intracellular accumulation of hyperphosphorylated tau protein forming neurofibrillary tangles, synaptic dysfunction,

oxidative stress, neuroinflammation, mitochondrial impairment, and progressive neuronal loss. These pathological changes primarily affect the hippocampus and cerebral cortex, regions responsible for learning, memory, and cognitive processing [3]. Despite extensive research, current therapeutic options for AD remain limited. Approved medications such as Donepezil, Rivastigmine, Galantamine, and Memantine provide only symptomatic relief and do not halt disease progression. Furthermore, systemic administration of these drugs is often associated with poor brain targeting, low bioavailability, peripheral side effects, and limited therapeutic efficacy due to the presence of the blood–brain barrier (BBB). The BBB is a highly selective physiological barrier formed by endothelial cells, astrocytes, and pericytes that regulates the transport of substances from the bloodstream into the central nervous system (CNS) [4]. Although essential for maintaining

brain homeostasis, the BBB significantly restricts the delivery of therapeutic agents to the brain. It is estimated that more than 98% of small-molecule drugs and nearly all large biomolecules are unable to cross the BBB effectively. Consequently, the development of efficient brain-targeted drug delivery systems has become a critical area of research in the management of neurodegenerative disorders, particularly Alzheimer disease. Nasal drug delivery offers several advantages, including rapid onset of action, avoidance of first-pass hepatic metabolism, ease of administration, improved patient compliance, reduced systemic adverse effects, and potential for self-administration [5]. These advantages make the nasal route particularly attractive for chronic neurodegenerative diseases such as Alzheimer disease, where long-term treatment is required. However, conventional nasal formulations such as solutions and sprays often suffer from rapid mucociliary clearance, short residence time, enzymatic degradation, and limited absorption. To overcome these limitations, medicated nasal gels have gained considerable attention. Nasal gels are semisolid formulations designed to increase residence time within the nasal cavity, enhance mucosal adhesion, improve drug absorption, and provide sustained drug release [6]. Alzheimer disease is a multifactorial neurodegenerative disorder involving complex molecular and cellular mechanisms. The disease progresses slowly over several years and is characterized by a continuum from preclinical stages to mild cognitive impairment and eventually severe dementia. Brain drug delivery remains one of the most challenging areas in pharmaceutical sciences due to the restrictive nature of the BBB and other CNS barriers. Traditional therapies often fail to achieve therapeutic concentrations within the brain, limiting treatment efficacy for neurological diseases. Advances in nanotechnology, targeted delivery systems, receptor-mediated transport mechanisms, and intranasal administration have significantly enhanced the potential for successful CNS drug delivery [7]. Nanocarriers such as liposomes, polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, dendrimers, and exosomes have demonstrated remarkable ability to improve brain targeting and therapeutic efficacy. Continued research focusing on safety, scalability, and clinical translation is expected to transform the management of neurological disorders and enable more effective treatment strategies in the

future. The term "gel" comes from "gelatin," and both "gel" and "jam" may be traced back to the Latin words "gelu" for "ice" and "gel" for "freeze" or "harden." Gels are described as semi-unbending structures in which the growth of the scattering medium is restrained by a three-layered arrangement of intertwined waste products or solvated dispersed section macromolecules [8-9]. The proposed work is focused on the formulation, development, and evaluation of a mucoadhesive in situ nasal gel for effective drug delivery through the nasal route. The study encompasses the selection of suitable polymers, gelling agents, and excipients capable of producing a formulation that remains in liquid form during administration and undergoes rapid gelation upon contact with the nasal environment. The present study aims to develop a medicated nasal gel formulation that can be conveniently administered into the nasal cavity and undergoes gelation to attain semisolid properties upon contact with the nasal mucosa. The specific objectives is enhance the mucoadhesive properties of the formulation, thereby promoting prolonged retention within the nasal cavity. Its also enhance drug delivery to the brain through the nose-to-brain pathway, thereby increasing drug concentration in the central nervous system and improving therapeutic efficacy.

Material and Methods

Preparation of Standard Calibration Curve of Selegiline Hydrochloride: An accurately weighed quantity of Selegiline hydrochloride (50 mg) was transferred into a 50 mL volumetric flask and dissolved in phosphate buffer (pH 6.4). The solution was sonicated for 20 minutes to ensure complete dissolution and the volume was adjusted to the mark with the same buffer to obtain a primary stock solution (Stock-I) having a concentration of 1000 µg/mL. Subsequently, 1 mL of Stock-I was transferred into a 100 mL volumetric flask and diluted to volume with phosphate buffer (pH 6.4), followed by sonication for 20 minutes, to obtain a secondary stock solution (Stock-II) with a concentration of 10 µg/mL. Aliquots of Stock-II corresponding to 1.0, 2.0, 3.0, 4.0, and 5.0 mL were accurately transferred into separate 10 mL volumetric flasks and diluted up to the mark with phosphate buffer (pH 7.4) to obtain solutions containing Selegiline hydrochloride at concentrations of 10, 20, 30, 40, and 50 µg/mL, respectively. The absorbance of each prepared solution was measured at 260 nm using a UV-Visible spectrophotometer, with phosphate buffer (pH 6.4) serving as the blank. A

standard calibration curve was constructed by plotting absorbance against the corresponding drug concentration, and the linearity of the method was evaluated from the resulting calibration plot [10-11].

Preparation of Gel Base: The gel base formulations were prepared using varying concentrations of Carbopol 934 and sodium carboxymethyl cellulose (sodium CMC) as gelling polymers. The required quantities of methyl paraben sodium, glycerine, and polyethylene glycol (PEG) were dissolved in distilled water under continuous stirring. Subsequently, Carbopol 934 or sodium CMC along with polyvinyl pyrrolidone (PVP) was added slowly to ensure uniform dispersion. After complete hydration of the polymers, triethanolamine was added gradually to neutralize the dispersion and facilitate gel formation. The prepared gel bases were transferred into aluminum collapsible tubes, sealed, labeled, and stored for further evaluation [12].

Table 1: Formulation of various composition of gel base

Ingredient	GB1	GB2	GB3	GB4
Carbopol 934 (g)	1	2	–	–
Sodium CMC (g)	–	–	1	2
PVP (mg)	50	50	50	50
Methyl Paraben Sodium (mg)	75	75	75	75
Glycerine (mL)	5	5	5	5
Polyethylene Glycol (PEG) (mL)	5	5	5	5
Triethanolamine (mL)	1	1	1	1

Evaluation of Gel Base: The optimized gel base containing Carbopol 934 (1.5 g), PVP (50 mg), methyl paraben sodium (75 mg), glycerine (5 mL), polyethylene glycol (PEG, 5 mL), and triethanolamine (1 mL) was evaluated for its physicochemical properties.

Physical Appearance: The gel was visually inspected for color, transparency, consistency,

and overall appearance. The formulation was also assessed for smoothness and ease of application on the skin [13].

pH Determination: One gram of gel was dispersed in 100 mL of distilled water and allowed to equilibrate for 2 h. The pH was measured using a calibrated digital pH meter, and the mean of three determinations was recorded.

Extrudability: The gel was filled into collapsible aluminum tubes, and the force required to extrude a 0.5 cm ribbon of gel within 10 s was determined. Good extrudability was indicated by easy and uniform extrusion.

Viscosity: Viscosity was measured using a Brookfield viscometer at 2.5 rpm under ambient conditions. The recorded value reflected the flow characteristics of the gel [14].

Spreadability: Spreadability was evaluated using a glass slide apparatus. It was calculated using the equation $S = M \times L/T$, where M is the applied weight, L is the slide length, and T is the separation time. Higher spreadability indicated easier application.

Homogeneity and Grittiness: The gel was examined visually and microscopically for uniformity and the absence of lumps, aggregates, or undissolved particles. A homogeneous and grit-free formulation was considered suitable for topical application [15].

Preparation of topical nasal gel:

The preparation of Selegiline Hydrochloride nasal gels, seven formulations (SG1–SG7) were developed using Carbopol 934 as the gelling polymer. Each formulation contained 100 mg of Selegiline Hydrochloride, 1.5 g of Carbopol 934, 50 mg of PVP, 75 mg of methyl paraben sodium, 5 mL of glycerine, 5 mL of PEG, and 1 mL of triethanolamine, with distilled water added to make a final weight of 100 g. The formulations were differentiated based on the type and concentration of permeation-enhancing essential oils incorporated into the gel matrix. Formulations SG1–SG4 contained neem oil at concentrations of 0.5, 1.0, 1.5, and 2.0 mL, respectively, whereas formulations SG5–SG7 incorporated clove oil at concentrations of 0.5, 1.0, and 1.5 mL, respectively. Almond oil was not included in these formulations. Carbopol 934 was selected due to its excellent mucoadhesive and gel-forming properties, which facilitate prolonged nasal residence time and sustained drug release. PVP served as a stabilizing and film-forming agent, while glycerine and PEG acted as humectants and plasticizers, improving gel consistency and patient acceptability.

Triethanolamine was used to neutralize Carbopol and adjust the gel pH to an acceptable range for nasal administration. The incorporation of neem and clove oils was intended to enhance drug permeation across the nasal mucosa and improve nose-to-brain delivery of Selegiline Hydrochloride. The prepared formulations were subsequently evaluated for their physicochemical characteristics, mucoadhesive properties, drug release behavior, and permeation performance [16].

Table 2: Factor Levels

Factor	Level -1	Level 0	Level +1	Level +2
Concentration of Enhancer (mL)	0.5	1	1.5	2
Type of Enhancer	Neem Oil	—	Clove Oil	—

Table 3: A various composition of different topical nasal gel

Formulation Code	Factor A: Permeation Enhancer	Factor B: Concentration (mL)	Carbopol 934 (g)	PVP (mg)	Methylparaben Sodium (mg)	Glycerine (mL)	PEG (mL)	Triethanolamine (mL)	Distilled Water (g)
SG1	Neem Oil	0.5	1.5	50	75	5	5	1	100g
S	N	1	1.	5	7	5	5	1	1

G2	Neem Oil		5	0	5				00g
SG3	Neem Oil	1.5	1.5	50	75	5	5	1	100g
SG4	Neem Oil	2	1.5	50	75	5	5	1	100g
SG5	Clove Oil	0.5	1.5	50	75	5	5	1	100g
SG6	Clove Oil	1	1.5	50	75	5	5	1	100g
SG7	Clove Oil	1.5	1.5	50	75	5	5	1	100g
SG8*	Clove Oil	2	1.5	50	75	5	5	1	100g

Characterization of Topical Nasal Gel

Physical Evaluation: The prepared gel formulations were visually inspected for color, appearance, consistency, homogeneity, and the presence of any aggregates. Homogeneity was assessed by visual examination before filling the formulations into suitable containers. The formulations were also evaluated for smoothness and overall appearance to ensure uniformity and aesthetic acceptability.

Globule Size and Polydispersity Index (PDI): The mean globule size and polydispersity index of the formulations were determined using Dynamic Light Scattering (DLS) analysis. These parameters were evaluated to assess the uniformity of droplet distribution and stability of the gel system. A lower PDI value indicated a narrower size distribution and better formulation homogeneity [17].

pH Determination: The pH of the formulations was measured using a calibrated digital pH meter. The pH values were recorded to ensure

compatibility with the nasal mucosal environment and to minimize the risk of irritation upon administration.

Viscosity Measurement: The viscosity of the gel formulations was determined using a Brookfield cone-and-plate viscometer equipped with spindle No. 7. The instrument was connected to a thermostatically controlled water bath maintained at $25 \pm 1^\circ\text{C}$. An adequate quantity of gel was placed in a suitable container, and viscosity measurements were recorded at a spindle speed of 2.5 rpm. The viscosity values were expressed in centipoise (cP) [18].

Spreadability Study: Spreadability was determined using a modified extensometer apparatus based on the principles of slip and drag. Two grams of gel were placed between two glass slides, and a weight of 1 kg was applied for 5 min to obtain a uniform film. Subsequently, a weight of 100 g was attached to the upper slide, and the time required for the slide to move a distance of 7 cm was recorded. Spreadability was calculated using the following equation:

$$S = \frac{M \cdot L}{T}$$

where S is spreadability, M is the weight tied to the upper slide (g), L is the length moved by the slide (cm), and T is the time taken for separation (s). Higher spreadability values indicated better ease of application.

Drug Content Determination: One gram of gel formulation was accurately weighed and dissolved in methanol, followed by sonication for 1 h. The resulting solution was filtered through a $0.45 \mu\text{m}$ membrane filter, and the drug content was quantified using a UV-Visible spectrophotometer at 260 nm [19].

In Vitro Permeation Studies: In vitro permeation studies were performed using Franz diffusion cells (diffusion area: 3.8 cm^2) fitted with excised porcine ear skin as the permeation membrane. The receptor compartment was filled with 75 mL phosphate buffer (pH 6.8) maintained at $37 \pm 0.5^\circ\text{C}$ and stirred continuously at 100 rpm. The skin was mounted between donor and receptor compartments with the stratum corneum facing the donor side and equilibrated for 30 min. Gel formulation equivalent to 100 mg was applied to the donor compartment. Samples (1 mL) were withdrawn at predetermined intervals up to 24 h and replaced with fresh buffer. Drug concentration was determined spectrophotometrically at 260 nm. At the end of the study, the amount of drug retained on and within the skin was quantified following extraction with methanol and subsequent UV analysis.

Drug Release Kinetic Analysis: The in vitro release data were fitted to various kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer-Peppas models, to elucidate the mechanism and kinetics of drug release from the gel formulations [20-21]

Result and Discussion

Evaluation of gel base formulation: All gel formulations were visually inspected and found to be smooth, elegant, and free from phase separation. Carbopol-based formulations (GB1 and GB2) exhibited clear translucent appearance, whereas Sodium CMC-based formulations (GB3 and GB4) appeared slightly opaque. The pH values of all formulations ranged from 6.6 to 6.8, indicating compatibility with skin pH and suitability for topical application without causing irritation. All formulations showed satisfactory extrudability from collapsible tubes. GB1 and GB3 exhibited excellent extrudability due to their comparatively lower viscosity, while GB2 and GB4 showed good extrudability owing to higher polymer concentration. Viscosity increased with increasing polymer concentration. GB2 showed the highest viscosity due to the presence of 2 g Carbopol 934, followed by GB4 containing 2 g Sodium CMC. The results indicate efficient gel formation and desirable consistency. Spreadability was inversely proportional to viscosity. GB3 exhibited the highest spreadability, whereas GB2 showed comparatively lower spreadability because of its higher viscosity. Nevertheless, all formulations possessed acceptable spreading characteristics for topical use. All prepared gels were homogeneous in nature with no evidence of coarse particles or grittiness, indicating uniform distribution of ingredients throughout the gel matrix. Among all formulations, GB2 exhibited optimum viscosity, acceptable spreadability, suitable pH, and good extrudability, suggesting its potential as the most stable and effective gel formulation.

Table 3: Various results of optimized gel base

Parameter	GB1	GB2	GB3	GB4
Physical Appearance	Clear, smooth, translucent	Clear, highly viscous translucent	Smooth, slightly opaque gel	Smooth, opaque and thick

	gel	gel		gel
pH				
Deter	6.7 ±	6.8 ±	6.6 ±	6.7 ±
minati	0.05	0.04	0.03	0.05
on				
Extrud	Excele	Good	Excele	Good
ability	nt		nt	
Viscosi	18,250	28,450	14,780	22,360
ty (cP)	± 125	± 210	± 145	± 180
Spread				
ability	24.5 ±	20.3 ±	26.8 ±	22.1 ±
(g·cm/s	0.8	0.7	0.9	0.8
)				
Homog	Homog	Homog	Homog	Homog
eneity	eneous,	eneous,	eneous,	eneous,
and	no	no	no	no
Grittine	grittine	grittine	grittine	grittine
ss	ss	ss	ss	ss

Evaluation parameter of topical nasal gel:

Globule Size and Polydispersity Index (PDI): The globule size of the prepared formulations ranged from 176.3 ± 3.5 to 218.6 ± 5.4 nm, indicating successful preparation of nanosized systems. An increase in permeation enhancer concentration resulted in a gradual reduction in globule size. Formulation SG8 containing 2 mL clove oil exhibited the smallest globule size (176.3 nm) and lowest PDI (0.248), indicating a highly uniform distribution. All formulations showed PDI values below 0.35, confirming acceptable homogeneity and stability of the dispersed system.

pH Determination: The pH of all formulations was found between 6.12 ± 0.03 and 6.34 ± 0.03 , which falls within the acceptable physiological range of the nasal cavity (5.5–6.5). The results indicate that the formulations are unlikely to cause irritation or discomfort upon intranasal administration.

Viscosity Measurement: Viscosity values ranged from 4328 ± 34 to 4520 ± 48 cPs. Slight reductions in viscosity were observed with increasing concentrations of permeation enhancers, possibly due to interactions between the oil phase and Carbopol gel matrix. Nevertheless, all formulations maintained

sufficient viscosity to ensure prolonged nasal residence time and minimize mucociliary clearance.

Spreadability Study: Spreadability values ranged from 19.8 ± 0.7 to 23.6 ± 0.4 g·cm/s. Formulations containing higher concentrations of permeation enhancers showed improved spreadability, which may facilitate uniform distribution across the nasal mucosal surface. SG8 exhibited the highest spreadability, suggesting superior applicability.

Drug Content Determination: Drug content analysis demonstrated uniform distribution of selegiline throughout the gel matrix, with values ranging from $96.24 \pm 1.12\%$ to $99.42 \pm 0.76\%$. The low standard deviation indicates excellent mixing efficiency and minimal drug loss during formulation. SG8 showed the highest drug content (99.42%), reflecting efficient drug entrapment within the gel system.

In Vitro Permeation Studies: The cumulative drug permeation after 8 h varied from $71.42 \pm 1.84\%$ to $94.28 \pm 1.08\%$. Both neem oil and clove oil significantly enhanced permeation compared with lower concentrations. Formulations containing clove oil demonstrated superior permeation enhancement relative to neem oil at corresponding concentrations. SG8 exhibited the highest permeation (94.28%), followed by SG7 (90.37%). The enhanced permeation may be attributed to the ability of clove oil constituents to modify membrane lipid organization and improve drug partitioning across the nasal mucosa. SG8 > SG7 > SG4 > SG3 > SG6 > SG2 > SG5 > SG1

Drug Release Kinetic Analysis: Drug release data were fitted to various kinetic models including Zero-order, First-order, Higuchi, and Korsmeyer-Peppas equations. Among the models evaluated, the Higuchi model exhibited the highest correlation coefficient ($R^2 = 0.984–0.997$) for all formulations, indicating diffusion-controlled drug release from the hydrated polymeric matrix.

The release rate constant (K) increased from 0.172 h^{-1} for SG1 to 0.238 h^{-1} for SG8, demonstrating the positive influence of permeation enhancer concentration on drug diffusion. The Korsmeyer-Peppas release exponent (n) was found between 0.52 and 0.71, suggesting anomalous (non-Fickian) transport involving both diffusion and polymer relaxation mechanisms.

Table 4: Characterization of various parameter of selegiline hydrochloride topical nasal gel

Formulation	Globule Size (nm) Mean $\pm$ SD	PDI	pH	Viscosity (cP)	Spreading (g/cm ² /s)	Drug Content (%)	Cumulative Drug Permeation at 8h (%)	Release Rate Constant (K _h ⁻¹)	Best Fit Kinetic Model
SG 1	218.6 $\pm$ 5.4	0.312 $\pm$ 0.002	6.12 $\pm$ 0.003	4520 $\pm$ 48	19.8 $\pm$ 0.7	96.24 $\pm$ 1.12	71.42 $\pm$ 1.84	0.172	Higuchi
SG 2	205.3 $\pm$ 4.8	0.298 $\pm$ 0.001	6.18 $\pm$ 0.004	4485 $\pm$ 52	20.9 $\pm$ 0.8	97.31 $\pm$ 0.94	78.65 $\pm$ 1.56	0.188	Higuchi
SG 3	194.8 $\pm$ 3.9	0.284 $\pm$ 0.002	6.24 $\pm$ 0.005	4448 $\pm$ 44	21.7 $\pm$ 0.5	98.12 $\pm$ 1.03	84.76 $\pm$ 1.28	0.203	Higuchi
SG 4	189.	0.2	6.3	438	22.5 $\pm$ 0.6	98.6	88.42 $\pm$	0.21	Higuchi
SG 5	212.7 $\pm$ 5.1	0.305 $\pm$ 0.002	6.15 $\pm$ 0.004	4506 $\pm$ 46	20.3 $\pm$ 0.7	96.86 $\pm$ 1.06	75.84 $\pm$ 1.47	0.181	Higuchi
SG 6	198.4 $\pm$ 4.3	0.289 $\pm$ 0.001	6.22 $\pm$ 0.005	4457 $\pm$ 42	21.4 $\pm$ 0.6	97.94 $\pm$ 0.91	83.56 $\pm$ 1.33	0.199	Higuchi
SG 7	184.6 $\pm$ 3.8	0.261 $\pm$ 0.001	6.29 $\pm$ 0.004	4392 $\pm$ 36	22.8 $\pm$ 0.5	99.08 $\pm$ 0.82	90.37 $\pm$ 1.16	0.225	Higuchi
SG 8	176.3 $\pm$ 3.5	0.248 $\pm$ 0.001	6.34 $\pm$ 0.003	4328 $\pm$ 34	23.6 $\pm$ 0.4	99.42 $\pm$ 0.76	94.28 $\pm$ 1.08	0.238	Higuchi

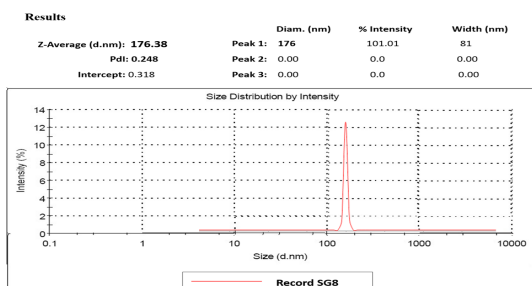


Figure 1: Particle sizeindex and PDI of selegiline hydrochloride topical nasal gel (SG8)

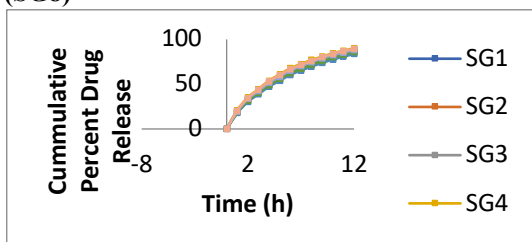


Figure 2: Zero-order plots for in-vitro drug release profile of prepared selegiline hydrochloride topical nasal gel (SG1-SG8)

Summary

The present study focused on the development and evaluation of Selegiline Hydrochloride topical nasal gel formulations intended for enhanced nose-to-brain drug delivery. Initially, different gel base formulations containing Carbopol 934 and Sodium CMC were prepared and evaluated. Among the tested gel bases, the Carbopol 934 formulation exhibited superior physicochemical characteristics, including suitable pH, viscosity, spreadability, homogeneity, and extrudability, and was therefore selected for further formulation development. Eight nasal gel formulations (SG1–SG8) were prepared using Carbopol 934 as the gelling polymer and varying concentrations of neem oil and clove oil as permeation enhancers. The formulations demonstrated satisfactory physicochemical properties with pH values ranging from 6.12 to 6.34, indicating compatibility with the nasal mucosa. Globule size analysis revealed nanosized particles (176.3–218.6 nm) with low polydispersity indices (<0.35), confirming uniform distribution and formulation stability. Viscosity and spreadability studies indicated that all formulations possessed adequate rheological characteristics for prolonged nasal residence and easy administration. Drug content ranged from 96.24% to 99.42%, demonstrating uniform drug distribution within the gel matrix. In vitro permeation studies showed that increasing concentrations of permeation enhancers

significantly improved drug permeation across the membrane. Clove oil produced greater permeation enhancement than neem oil, with formulation SG8 exhibiting the highest cumulative drug permeation (94.28% at 8 h), smallest globule size, lowest PDI, and highest drug content. Drug release kinetic analysis revealed that all formulations followed the Higuchi model, indicating diffusion-controlled release. The Korsmeyer–Peppas exponent suggested anomalous non-Fickian transport involving both diffusion and polymer relaxation mechanisms. Overall, formulation SG8 emerged as the optimized nasal gel, demonstrating excellent physicochemical properties and superior permeation performance, making it a promising candidate for intranasal delivery of Selegiline Hydrochloride.

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