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New-fangled approach in the management of Alzheimer by Formulation of Polysorbate 80 Coated Chitosan Nanoparticles of Rivastigmine for brain delivery and their *in vivo* evaluation.

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Abstract

Nanotechnology mediated drug delivery has been reported to enhance the drug efficacy, bioavailability, reduce toxicity and improve patient compliance by targeting the cells and tissues to produce desired pharmacological action. **Aim:** The purpose of the present study was to formulate and evaluate Polysorbate 80 Coated Chitosan Nanoparticles of Rivastigmine for brain delivery. **Methods:** Rivastigmine is short acting cholinesterase inhibitors (ChEI). Nanostructure mediated drug delivery enhances drug bioavailability, improves the timed release of drug molecules, and enables precision drug targeting. Because of its cationic charges, biocompatibility, and low toxicity, chitosan has been used as a vehicle system for genes, protein and drugs. The Nanoparticles were evaluated for size, shape, zeta potential, microscopy, transmission electron microscopy. Drug-polymer compatibility was determined using differential scanning calorimetry. The amount of drug entrapped within the Nanoparticles was determined spectrofluorometrically and *in vitro* drug release studies were done by spectrofluorometer. Test was used to evaluate *in vivo* activity of Rivastigmine Nanoparticles in mice. The drug-loading capacity obtained from the drug content analyses for the batches ranged from 43.48±3.5 to 52.62±4.31 depending upon the drug-to-polymer ratio. The drug loading of chitosan Nanoparticles (drug-to-polymer ratio 1:1) after coating with 1% Polysorbate 80 was 43.48±1.3. The particle size analysis showed that the mean particle size of drug-loaded Nanoparticles (drug-to-polymer ratio 1:1) was 45.16±1.56 nm.

Keywords: Nanoparticles, Chitosan, Stability study, Rivastigmine.

Introduction

Drug delivery to central nervous system is a major menace as multiple cerebral diseases like Alzheimer's, brain tumors, prison diseases are cropping up nowadays. Alzheimer's disease is a disorder that affects millions of older adults and causes more worry for people over 55 Years of age than any other condition. Alzheimer's disease is the most common form of dementia, a serious brain disorder that impacts daily living though memory loss and cognitive changes. Although not all memory loss indicates Alzheimer's disease one in ten people over 65 years of age and over half of those over 85 have Alzheimer's disease (AD). Currently 26 million people worldwide have this dementia. Symptoms of Alzheimer's disease usually develop slowly and gradually

worsen over time, progressing from mild forgetfulness to widespread brain impairment. Chemical and structure changes on the brain slowly destroy the ability to create, remember, learn reason and relate to others. Central Nervous system drug efficacy depends upon the ability of a drug to cross the Blood Brain Barrier (BBB) and reach therapeutic concentrations in the brain following systemic administration. The clinical failures of most of the potentially effective therapeutics to treat the central nervous system are often not due to a lack of drug potency but rather shortcomings in the method by which the drug id delivered. Hence, considering the importance of treatment Alzheimer's disease we made an attempt to target the anti Alzheimer's drug that is Rivastigmine (RT) in the brain by using poly (n-butylcyanoacrylate) [PBCA] and chitosan Nanoparticles.

The Nanotechnology is beginning to exert a significant impact in neurology. Nanoparticles are the simplest form of structures with sizes in the nm range. In principle any collection of atoms bonded together with a structural radius of <100 nm can be considered a Nanoparticles. These can include, e.g., fullerens, metal clusters (agglomerates of metal atoms), large molecules, such as proteins, and even hydrogen-bonded assemblies of water molecules, which exist in water at ambient temperatures. Nanoparticles are very commonplace in nature - for instance proteins exist in almost all biological systems, metal-oxide Nanoparticles are easily produced, etc.

Rivastigmine hydrogen tartrate (RHT), a USFDA approved reversible cholinesterase inhibitor is a candidate of choice, used in the treatment of Alzheimer's disease to treat mild to moderate dementia due to its favorable effect on patient's cognitive and behavioral symptoms. RHT is a non-competitive dual inhibitor, which inhibits the metabolism of both acetyl cholinesterase and butyrylcholinesterase and helps in enhancing acetylcholine level to moderate Alzheimer's disease by increasing central cholinergic function (Scarpini et al., 2003; Grossberg, 2003bioavailability of only 36% after 3 mg dose, leading to restricted entry into brain and lesser concentration at the target site (Fazil et al., 2012). Owing to its hydrophilic nature, oral delivery of RHT necessitates frequent oral dosing, resulting into accumulation of severe cholinergic side effects in the systemic circulation (Wilson et al., 2008; Yang et al 2013.

Chitosan is a biocompatible, bioactive, as well as biodegradable polymer that can be easily engineered. It is widely reported for preparation of micro and Nanoparticles. Because of its cationic charge, biocompatibility and low toxicity, chitosan has been used as a vehicle system for delivery of genes, proteins (including antibodies) and various categories of drugs. Chitosan was selected for present study because of its recognized mucoadhesive property and ability to enhance the penetration of large molecules across mucosal surface. Chitosan Nanoparticles were prepared by the ionotropic gelation process based on the interaction between the negative groups of sodium tripolyphosphate (TPP) and the positively charged amino groups of chitosan. Tripolyphosphate (TPP) was used to prepare chitosan Nanoparticles, because it is nontoxic, multivalent and able to form gelate through ionic interaction between positively charged amino groups of chitosan and negatively charged TPP. This process has been well reported for preparation of chitosan Nanoparticles for peptides and proteins delivery.

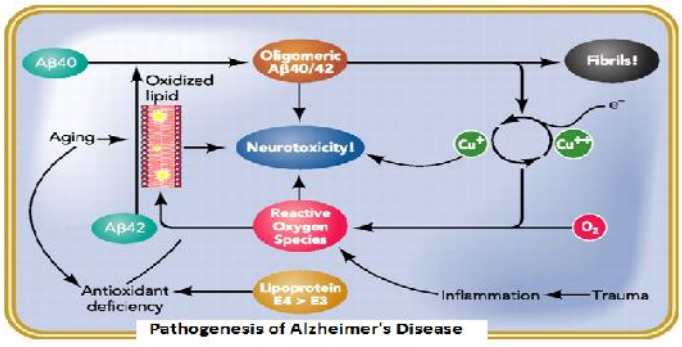

Fig:- 1 Pathogenesis of Alzheimer's disease.

Methods for the preparation of chitosan Nanoparticles

Chitosan Nanoparticles were first described in 1994, when Ohya and coworkers (1994) proposed the intravenous delivery of 5-fluorouracil, an anticancer drug, carried by chitosan Nanoparticles obtained by emulsification and cross-linking. Since then, these systems have been extensively studied for drug delivery purposes and the original formulation was either used for other applications, such as the incorporation of active substances in toothpastes (Liu et al. 2007a), or modified by the application of different preparation methods (Calvo et al. 1997, Erbacher et al).

1. Emulsification and cross-linking
2. Emulsion droplet coalescence
3. Emulsion solvent diffusion
4. Reverse micellisation
5. Ionic gelation and Polyelectrolyte complexation
6. Modified ionic gelation with radical polymerization
7. Desolvation.

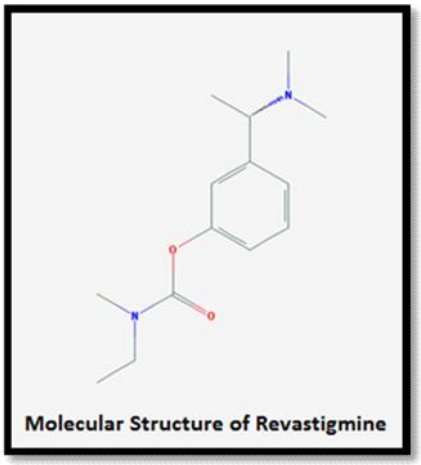

Fig.-2 Molecular structure of Rivastigmine.

These approaches which are often based on the design and engineering of a plethora of Nanoparticles entities with high specificity for brain capillary endothelial cells are currently being applied to early AD diagnosis and treatment. Alzheimer's disease may have numerous symptoms however cognitive and memory loss are not symptoms of normal aging and don't indicate Alzheimer disease. Other conditions can also cause mental decline. Symptoms that mimic early Alzheimer's disease may result from:-

1. CNS and other degenerative disorder.
2. Metabolic ailments
3. Substance induced conditions
4. Psychological factors and
5. Infections

Diagnosis:- since there is no single definitive medical test for identifying Alzheimer's disease arriving at the correct diagnosis can take time and patience. The most important step is to assess past and present functioning.

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Material and Method

Material

Rivastigmine as drug sample was obtained as gift sample from Sib Ram Pharma Pvt Ltd Mumbai. Disodium Hydrogen Phosphate and Potassium Dihydrogen Phosphate were got as gift sample from SRK Pharmaceuticals Mumbai. Chitosan (MW=250 KDa; Degree of deacetylation=80%) was a gift from India Sea Foods (Cochin, India). Sodium Tripolyphosphate was purchased from Central Drug House Ltd., New Delhi. All other chemicals were of analytical grade and were used without further purification.

Method

Preparation of chitosan Nanoparticles

Chitosan Nanoparticles containing the drug Rivastigmine were prepared by using the method of Spontaneous emulsification. Chitosan gel was prepared as following

a) Required quantity of chitosan (27 centipoises) and NaCl (2%) were dispersed in required quantity of (3% v/v) glacial acetic acid and stirred for 2 hrs continually to obtain chitosan gel.
b) Prepared solution was kept for overnight to get clear chitosan gel.
c) Drug Rivastigmine was dissolved separately in 5mL of Chitosan gel (drug to polymer ratio of 1:1, 1:2 and 1:3) under magnetic stirring.
d) Chitosan gel containing drug was added drop wise into 10mL of linseed oil containing 2% v/v of span 80 under magnetic stirring, added 5mL of acetone as drop wise (2mL/ min) in above solution.
e) Stir above solution for 1 hr while covering with aluminum foil.
f) 5mL of glutaraldehyde saturated toluene was added slowing and stir continue for 2 hrs.
g) Obtained Nanoparticles suspension was centrifuged at 5000 rpm and washed with toluene and then dried.
h) To get drug free Nanoparticles as placebo Nanoparticles were also prepared in the same manner by omitting the drug.

Coating of Polysorbate 80 to chitosan Nanoparticles

The coating of chitosan Nanoparticles (drug to polymer rartio 1:1) was performed according to the procedure described by Kreuter et al (2003). The drug loaded Nanoparticles were re-suspended in phosphate buffered saline at a concentration of 20mg/mL under constant straining. Then (relative to total suspension volume) Polysorbate 80 was added to give a final solution of 1% w/v polysorbate 80 and the mixture was incubated for 30 mints. The coated Nanoparticles were subjected to drug loading capacity, encapsulation efficiency, zeta potential measurement and *in vitro* release study.

Optimization of Formulation and Process Variables

Various formulation and process variables i.e. drug polymer ratio, stirring speed and stirring time which could affect the preparation and properties of Nanoparticles were identified and studied. The optimization was done on the basis of particle size and drug loading efficiency.

a.Optimization of Process Variables

1). Optimization of stirring speed

Stirring speed of the stirrer was varied from 100 to 300 rpm for preparation of CS-NPs using the optimized formulation parameters i.e. drug concentration (1mg/mL), quantity of polymer 5mL (1 mg/ml). The particle size and process yield were determined which are recorded in Table 1.

Table 1: Effect of stirring speed on particle size and Process yield of Chitosan Nanoparticles

Formulation code	Stirring Speed (rpm)	Particle size (nm)	Process Yield ± (SD)
F-1A	100	55.42±1.10	82.23±0.93
F-1B	200	53.32±1.06	83.51±0.25
F-1C	**300**	**48.68±0.97**	**84.47±0.22**

Values are expressed as Mean ±SD, N=3

2). Optimization of stirring time

Stirring time of the stirrer was varied from 2 to 4 hour for nanoparticles preparation F-1C using the optimized formulation parameters i.e. drug concentration (1mg/mL), quantity of polymer 5 mL (1 mg/ml) and stirring speed 300 rpm. The particle size and process yield were determined which are recorded in Table .2.

Table 2: Effect of stirring time on particle size, PDI and Process Yield of chitosan Nanoparticles

Formulation code	Stirring time (hour)	Particle size (nm)	Process Yield ± (SD)
F-1D	2	56.32±1.12	81.51±0.25
F-1E	3	51.72±1.03	82.89±0.58
F-1F	**4**	**45.62±0.91**	**86.32±0.63**

Values are expressed as Mean ±SD, N=3

b. Optimization of Formulation Variables

1). Optimization of drug polymer ratio of Rivastigmine loaded CS-NPs on the basis of particle size and process yield

Drug polymer ratio was varied from 1:1; 1:2 and 1:3 for Nanoparticles preparation F-1F using the optimized formulation parameters i.e. drug concentration (1 mg/ml), quantity of polymer 5 mL (1 mg/ml) and stirring speed 300 rpm. The particle size and process yield were determined which are recorded in Table 3.

Table 3: Effect of drug polymer ratio on particle size, LC, EE and process yield of chitosan Nanoparticles

Formulation code	Particle Size (nm)	Drug Polymer ratio (D:P)	Loading Capacity (%)	Entrapment Efficiency (%)	Process Yield ± (SD)
F-1G	**41.12±0.82**	**1:1**	**47.32±1.41**	**85.3ï3.1**	**87.51±0.25**
F-1H	43.58±0.87	1:2	46.72±1.40	81.5±3.3	85.89±0.58
F-1I	45.36±0.90	1:3	52.62±1.57	75.1±4.2	91.32±0.63

Values are expressed as Mean ±SD, N=3

Preparation of Optimized Formulation

On the basis of formulation and process variables, the optimized Nanoparticles formulation was prepared and its characteristics are recorded in Table 4.

Table 4: Characterized formulation of CS NPs and PS80 Coated CS NPs

Formulation Code	Particle size (nm)	Zeta potential (mV)	Loading Capacity (%)	Entrapment Efficiency (%)	Process Yield ± (S.D)
CS-NPs	43.72±0.87	37.25±1.2	45.55±1.36	85.3±3.5	87.89±0.58
PS80-NPs	45.16±0.90	35.08±1.5	43.48±1.30	83.26±3.1	85.63±0.48

chitosan: 5 mL (1 mg/ml), Stirring Speed: 300 rpm and Stirring: 4 hour, Drug Concentration: 1.0 mg/mL (5 mL), Values are expressed as Mean ±SD, N=3.

Characterization of Optimized Nanoparticles

The surface morphology of the prepared NPs were determined for by using transmission electron microscopy (TEM). The nanosuspension samples were prepared by dispersing a small amount of NPs into distilled water. A drop of nanosuspension was placed on a paraffin sheet and carbon coated grid was placed on sample and left for 1 min to allow NPs to adhere on the carbon substrate.

The remaining suspension was removed by adsorbing the drop with the corner of a piece of filter paper. Then the grid was placed on a drop of phosphotungstate for 10s. The remaining solution was removed by absorbing the liquid with a piece of filter paper and the sample was air dried. The sample was examined by TEM (Hitachi H-7500).

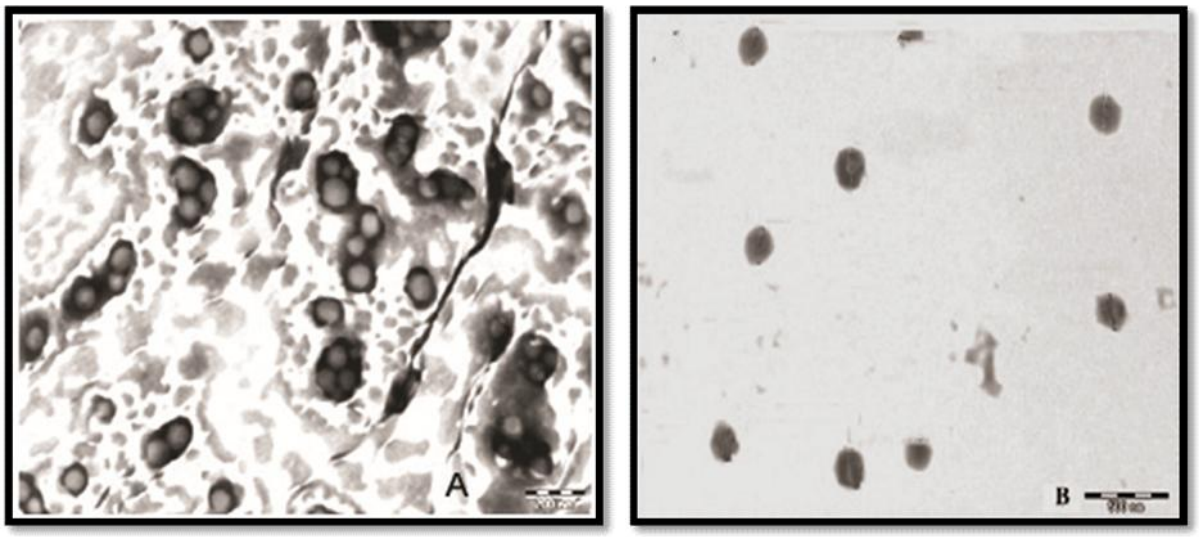

Fig. 3-TEM photographs of (A) PBCA DNP (B) CS DNPs

The particle size, particle size distribution, Polydispersity index, and zeta potential were determined by Zetasizer Nano ZS, (Malvern Instruments Ltd, Worcestershire, UK). Measurements were performed using Standard laser 4 mW He–Ne, 633 nm, and room temperature 25˚C at fixed angle of 90˚. The sample volume used for the analysis was kept constant i.e., 1 ml. The instrument is equipped with appropriate software for analysis of particle size, zeta potential and polydispersity index.

Determination of the Loading Capacity, Encapsulation Efficiency and Process Yield of NPs

The EE and LC of NPs were determined by separation of NPs from the aqueous medium containing non-associated RT by centrifugation at 15,000 rpm at 4˚C for 45 min. The amount of free RT in the supernatant was measured by UV spectrophotometer at 261 nm. The EE and LC of CS-RT NPs were calculated as per equations given below with all the measurements were performed in triplicate and averaged.

$$EE = \frac{\text{TOTAL DRUG} - \text{FREE DRUG}}{\text{TOTAL DRUG}} \times 100 \quad (1)$$

$$LC = \frac{\text{TOTAL DRUG} - \text{FREE DRUG}}{\text{NANOPARTICLES WEIGHT}} \times 100 \quad (2)$$

The process yield was calculated from the weight of dried NPs recovered (W1) and the sum of the initial dry weight of starting materials (W2) using the following formula:-

$$\text{Process Yield (\%)} = W1/W2 \times 100 \quad (3)$$

In vitro Release Study

The in vitro release profile of CS NPs and CS NPs solution were performed using dialysis sacs. The drug loaded CS NPs and PS80 coated CS NPs were placed in pretreated dialysis sacs, which were immersed into 100 ml of phosphate buffer solution, pH 7.4, at 37˚C and magnetically stirred at 50 rpm. At selected time intervals, aliquots were withdrawn from the release medium and replaced with the same amount of phosphate buffer. The samples were analyzed in triplicate using HPLC. The HPLC determination was performed using reverse phase Phenomenex C column (25 cm 4.6 i.d., 5 lm). The mobile phase consisted of 10 mM ammonium hydroxide (pH 10.50): acetonitrile (30:70 v/v %) at a flow rate of 1 ml/min. The peak detection was performed at 215 nm (LaPorte and Wu, 2007) and data plotted in Fig 4.

Table- 5 % drug Release from CS DNPs and PS80-CS DNPs in pH 7.4 Phosphate buffer

Time (h)	CS NPs	PS80-CS NPs
0	0.87±0.5	0.79±0.6
0.5	18.29±0.4	17.03±0.6
1	29.57±0.7	28.18±1.2
2	38.42±1.1	36.89±2.5
3	48.79±1	46.03±2.3
4	56.38±2.1	53.17±1.5
8	68.09±0.2	63.25±2.1
12	72.45±1.5	67.58±1.2
16	75.56±1.8	70.22±1.9
19	78.23±2.3	72.11±2.1
24	81.01±2.1	75.18±1.8

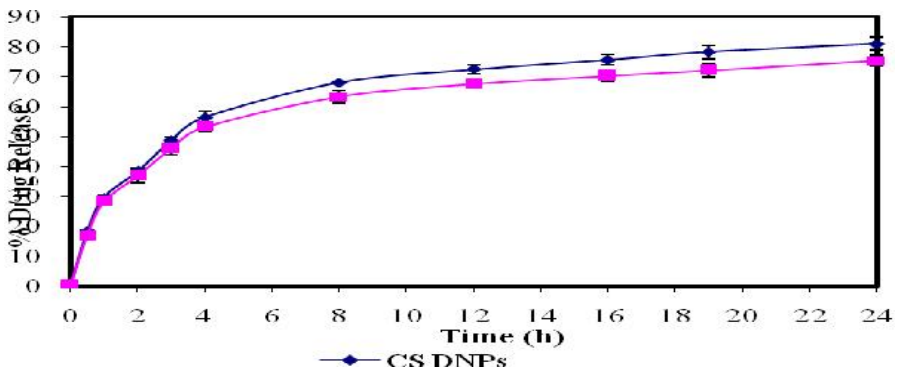

Fig. 4- Cumulative % Drug Release from CS DNPs and PS80-CS DNPs in pH 7.4

The in vitro release of Rivastigmine from all the drug loaded batches of PBCA-NPs were studied separately as per the procedure described by Marchal-Heussler et al. (1990) in pH 7.4 phosphate buffer. Nanoparticles coated with polysorbate 80 (drug polymer ratio 1:1) were also subjected to the in vitro release studies. Nanoparticles equivalent to 1 mg of the drug Rivastigmine was placed in a cellulose dialysis bag (cut-off 5 kDa, Himedia, India), and to this a little amount of dissolution media was added, which was thensealed at both ends. The dialysis bag was dipped into the receptor compartment containing the dissolution medium, which was stirred continuously at 100 rpm and maintained at 37°C. The receptor compartment was closed to prevent evaporation of the dissolution medium. Samples were withdrawn at regular time intervals and the same volume was replaced with fresh dissolution medium. The samples were measured by UV Spectrophotometer (Thermofischer) at a wavelength 210 nm against dummy Nanoparticles as reagent blank which had also been prepared and treated similar to the drug loaded Nanoparticles.

Stability Testing

Chitosan and PBCA DNPs formulation was subjected to stability studies. The formulation was stored at 4±2°C and 37±2°C. Change in the particle size and residual drug content after time interval of 10, 20, 30, 45 and 60 days were determined.

The average particle size of the Nanoparticles was found to increase on storage, which may be due to aggregation of particles. This effect was encountered lower in the case of formulation stored at 4^oC. This signifies that storage temperature can regulate aggregation and hence ideal storage temperature for Nanoparticles is 4^oC.

By keeping the initial drug content 100%, the determination of percentage residual drug in Nanoparticles showed that 4-5% of drug was lost from the formulation within 60 days, which were stored at 4^oC and significantly more (5-8%) drug was lost from those stored at 37^oC, which could be due to more leaching of the drug from Nanoparticles at 37^oC. Data obtained from stability tests indicated that Nanoparticles formulations stored at 4^oC were more stable than those stored at room temperature.

In vivo Studies

The *in vivo* studies are important in evaluating the therapeutic efficacy of designed dosage form. The *in vivo* performance is the preliminary step for clinical evaluation of a dosage form.

Rivastigmine in conventional dosage forms after oral administration is poorly bioavalable and very less quantity of drug reached to the circulation. Therefore, i.v. route for drug delivery is preferred. But, by i.v route, the drug reaches to all parts of body and causes some side effects. A successful brain targeted drug delivery system is one which remains intact in physiological environment of brain and subsequently releases the drug in the brain. In vivo performance of drug loaded Nanoparticles (DNPs) and drug loaded PS80 coated Nanoparticles (PS80-DNPs) was determined in mice for the targeted delivery of Rivastigmine to brain and various organs. All experiments were performed after taking approval from the Institutional Animal Ethics Committee of Bhagyoday Tirth Pharmacy College, Sagar (M.P.)

Bio Distribution Studies

Blood sample was collected through cardiac puncture in a centrifuge tube which contains heparin (anticoagulant) and centrifuged at 5000 rpm for 10 minutes. Supernatant was collected, then added 2ml of 0.4% ortho-phosphoric acid and was deprotenized with equal amount of acetonitrile for half an hour to precipitate proteins. The precipitated proteins were separated by centrifugation at 5000rpm for 10min and supernatant was collected and filtered through 0.45µm membrane filter. Mixture of orthophosphoric acid: acetonitrile (60:40 *v/v*) was used as the mobile phase. Serum with an appropriate volume of a known amount of drug at a concentration range 1000ng – 15000ng/ml of serum and filtered. The filtrate (25µl) was injected into a reverse phase C_{18} 150 X 46 mm HPLC column and the eluents were monitored

at 210 nm with a flow rate 1.0 ml / min. The peak area of drugs were recorded, the regression of plasma serum concentration of the drug over its peak areas were calculated using the least square method of analysis. The retention time of rivastigmine was recorded at 4.3 min.

Table 6: Calibration curve of Rivastigmine in blood serum at $^{a}_{max}$ 210 nm

Concentration (ng/ml)	Peak Area (Observed)	Peak Area (Regressed)	Equation of line:
1000	18280	14316	y = 20.552x - 4721.4 r^2=0.998
2000	31750	35046	
3000	52659	55776	
4000	72576	76506	
5000	100867	97236	
10000	207233	200886	
15000	300952	304536	

The concentration of Rivastigmine in different organs was estimated by HPLC. Experimental results shows that the concentration of Rivastigmine (ng/mL) achieved in different organs such as liver, spleen, lungs, and kidneys after intravenous injection of Rivastigmine free drug, Rivastigmine bound to chitosan Nanoparticles, and Rivastigmine bound to chitosan Nanoparticles coated with 1% Polysorbate 80. In different organs; the concentration of Rivastigmine varies depending on which form it was administered. The concentration of Rivastigmine achieved after the intravenous administration of a free drug in the liver, spleen, lungs and kidneys was 273.0±18.1, 261.6±25.9, 655.9±33.9 and 863.9±118.9 ng/ml respectively. But when the drug Rivastigmine was administered as Nanoparticles the concentration in the liver, spleen, lungs and kidneys was 408.2±42.1, 382.8±37.5, 691.1±37.7 and 582.5±55.6 ng/ml respectively. The concentration of Rivastigmine in the liver, spleen, lungs and kidneys, after the intravenous administration of Rivastigmine bound to Nanoparticles which were further coated with polysorbate 80, was 286.5±23.2, 327.6±43.8, 717.7±57.1 and 674.2±53.2 ng/ml respectively. But in brain the Rivastigmine concentration was significantly increased, when it was bound to poly (n-butylcyanoacrylate) Nanoparticles and coated with polysorbate 80 in comparison with the free drug. The concentration of Rivastigmine achieved in the brain when Rivastigmine was administered alone, when it was bound to Nanoparticles, and when the Nanoparticles bound drug was coated with polysorbate 80 was 44.8±3.7, 54.8±3.4 and 171.1±10.0 ng/ml respectively. The poly (n-butylcyanoacrylate) Nanoparticles coated with 1% polysorbate 80 increased the concentrations of Rivastigmine in the brain by 3.82 fold in comparison with the free drug Rivastigmine.

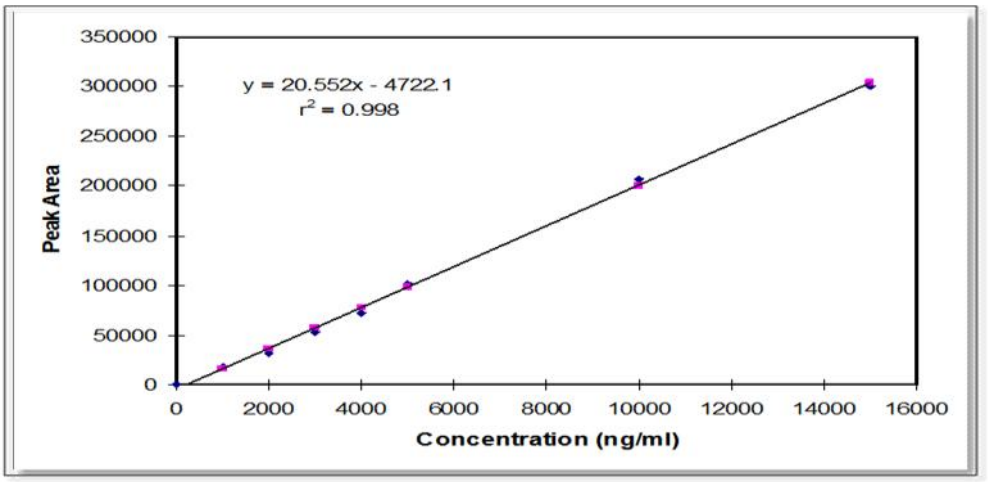

Fig. 5- Linearly regressed calibration curve of drugs in serum at λ_{max} 210.

Table: 7 Rivastigmine concentrations (ng/mL) in different organs after intravenous injection of chitosan Nanoparticles formulations

S. No.	Organs	Rivastigmine Concentration (ng/ml)		
		Plain Drug	CS DNPs	PS80-CS DNPs
1	Brain	38.8±3.7	52.8±3.4	168.1±10.0
2	Liver	316.88±35.18	587.21±53.53	364.22±20.06
3	Spleen	275.68±16.68	531.04±58.52	479.24±30.93
4	Lung	779.94±57.46	838.99±59.35	868.64±59.39
5	Kidney	1063.13±96.22	716.57±103.98	618.22±55.77

Results and Discussion

Chitosan Nanoparticles of the drug Rivastigmine with different drug-to-polymer ratios (1:1, 1:2, and 1:3) were prepared by spontaneous emulsification. Table 4 shows the process yield, percentage drug loading, encapsulation efficiency and particle size of chitosan Nanoparticles. Yields of production ranged between 81.51±0.25 and 91.32±0.63 depending on the drug-topolymer ratio used. The Nanoparticles prepared using a drug-topolymer ratio of 1:1 showed the highest value. The drug-loading capacity obtained from the drug content analyses for the batches ranged from 43.48±3.5 to 52.62±4.31 depending upon the drug-to-polymer ratio. The drug loading of chitosan Nanoparticles (drug-to-polymer ratio 1:1) after coating with 1% Polysorbate 80 was 43.48±1.3. The particle size analysis showed that the mean particle size of drug-loaded Nanoparticles (drug-to-polymer ratio 1:1) was 45.16±1.56 nm. The mean zeta potentials of chitosan Nanoparticles that contain Rivastigmine coated with 1% Polysorbate 80 and without coating were 35.08±1.5 and 37.25±1.2 mV, respectively. The cumulative percentage release of the drug Rivastigmine from chitosan Nanoparticles varied from 67.58%±1.2% to 81.01%±2.1 depending upon the drug-to-polymer ratio for 24 hours. But the cumulative percentage release of Rivastigmine from the coated Nanoparticles (drug-to-polymer ratio 1:1) was 74.53±1.2 for 12 hours.

Conclusion

The present study was aimed at developing and exploring the use of Nanoparticles for delivery of antialzheimer drug, Rivastigmine. For this study, drug loaded PS80 coated Chitosan and PBCA NP's were tested for storage stability to provide, evidence on how the quality of a formulation varies with time under the influence of temperature.

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