

INSTITUTE OF PHARMACY

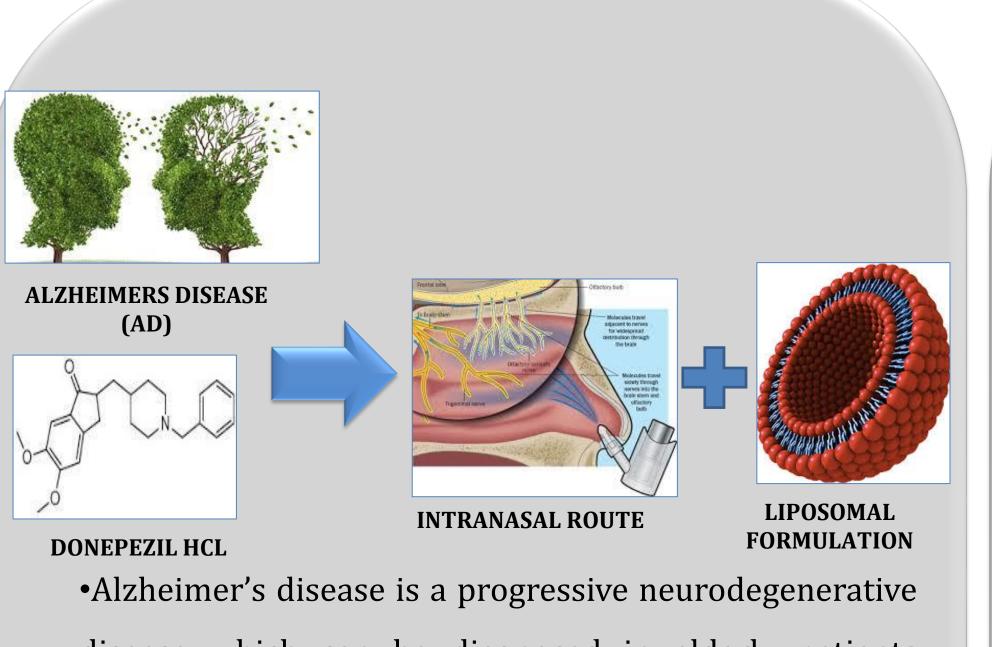
NAAC ACCREDITED 'A' GRADE

# NOSE TO BRAIN TARGETED DELIVERY OF DONEPEZIL LIPOSOME BASED IN-SITU GEL IN TREATMENT OF ALZHEIMER'S DISEASE

Amarjitsing Rajput<sup>1\*,</sup> Alex George<sup>2</sup>, Shital Butani<sup>1</sup>

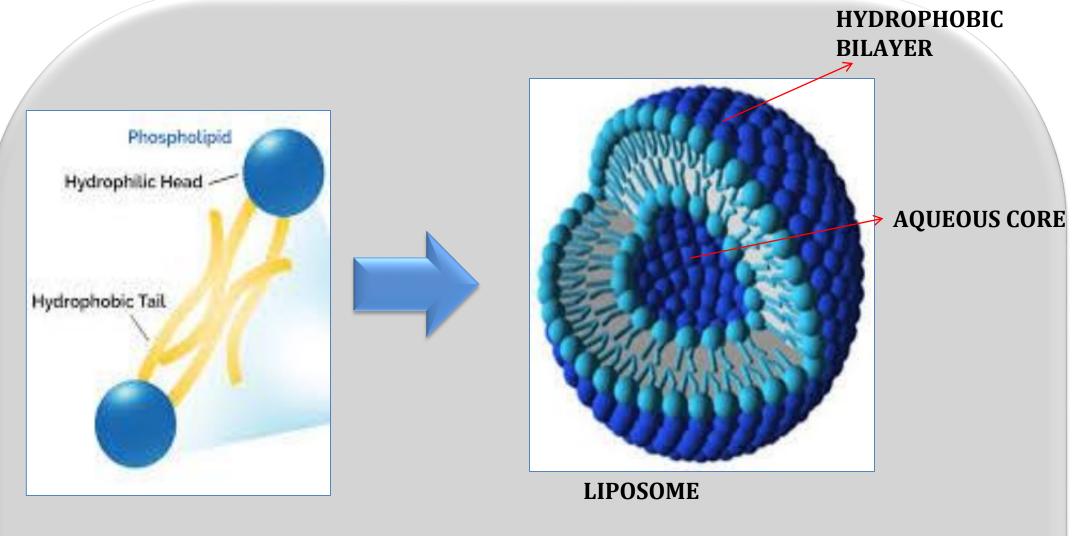
<sup>1</sup>Institute of Pharmacy, Department of Pharmaceutics, Nirma University, S.G.Highway, Ahmedabad, Gujarat, India. <sup>2</sup> Cadila Healthcare Limited, PTC, Moraiya, Ahmedabad, Gujarat, India.

#### INTRODUCTION



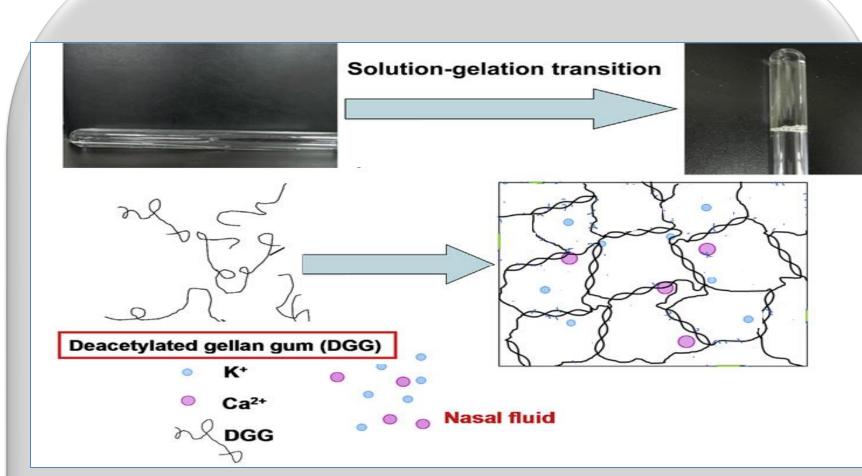
- disease which can be diagnosed in elderly patients affected with memory loss.
- •Donepezil hydrochloride is an acetylcholinesterase inhibitor and increases the acetylcholine concentration the brain.

#### LIPOSOMES



- •Liposomes are spherical vesicle structures composed of a uni or multilamellar lipid bilayer.
- •Liposomes are useful drug delivery carriers due to biocompatible and nontoxic nature, can deliver both hydrophilic and lipophilic drug molecules and transport them across biological membranes and the blood brain barrier.

## **IN-SITU GEL**



- •In-situ gel is in a sol form before administration in the body and transform into a gel form after reaching to the target site
- •Advantages include sustain drug action, reduce the dose and frequency of administration and improve a patient compliance

## PREPARATION OF LIPOSOMES

MLVs Formation by Ethanol Injection

Particle size reduction by HPH

Dialysis: Removal of Extraliposomal Buffer

Active drug loading

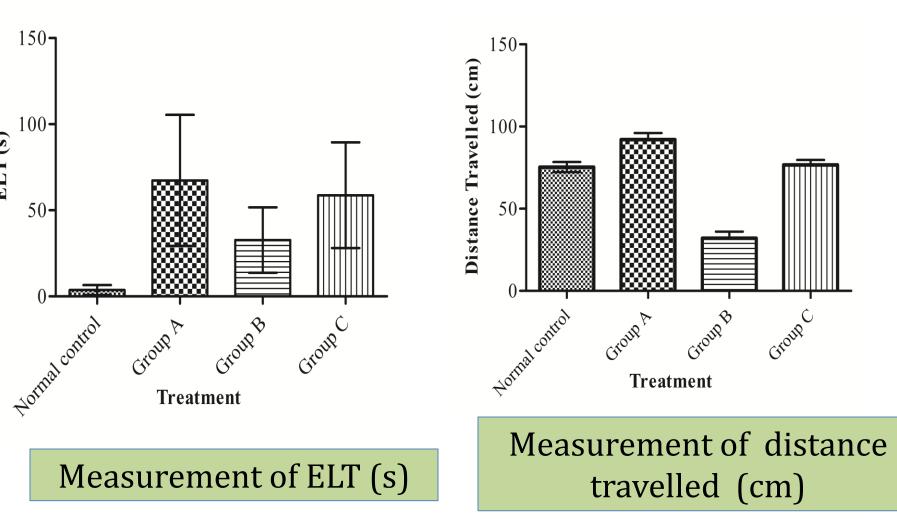
#### LOADING METHODS STUDY

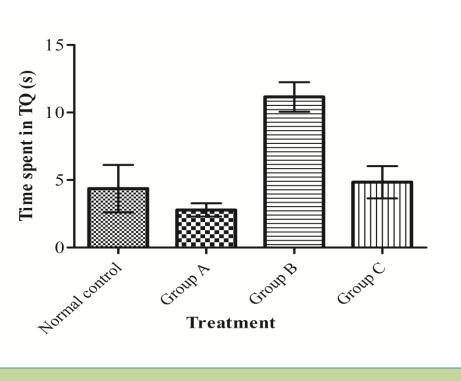
Parameter	Active Loading	Passive Loading
Particle size (nm)	96.82	100.8
Entrapment efficiency (%)	86.25	31.25
PDI	0.123	0.192

AMMONIUM SULPAHTE

**CONCENTRATION STUDY** 

#### PHARMACODYNAMIC STUDY





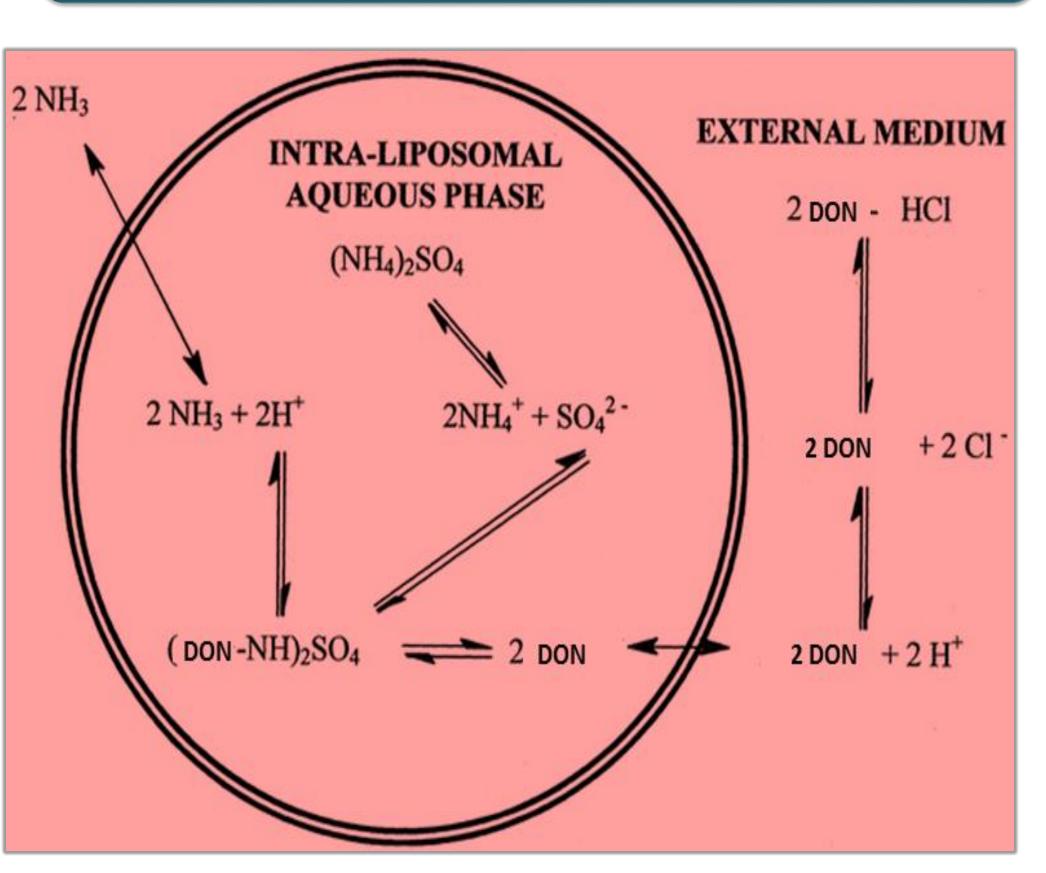
Measurement of time spent in target quadrant (s)

Measurement of number

Group A- DON Group A- Scopol. Indu. amnesia Lipo based gel of annulus crossings Group A- DON Mkt

tablet

## ACTIVE LOADING OF DONEPEZIL HCL

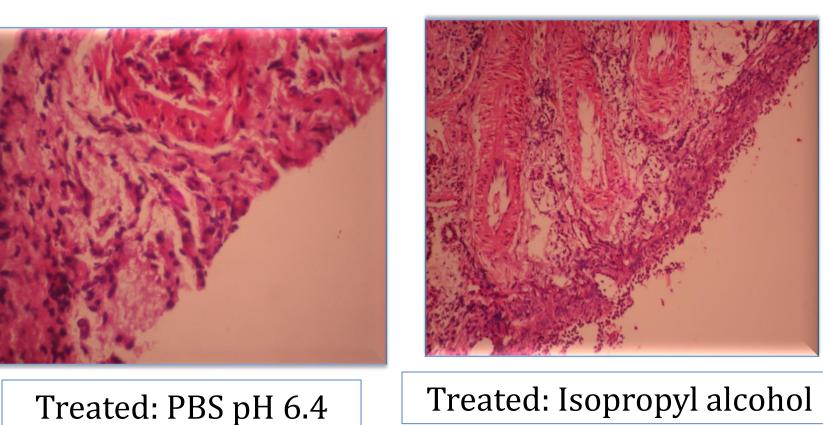


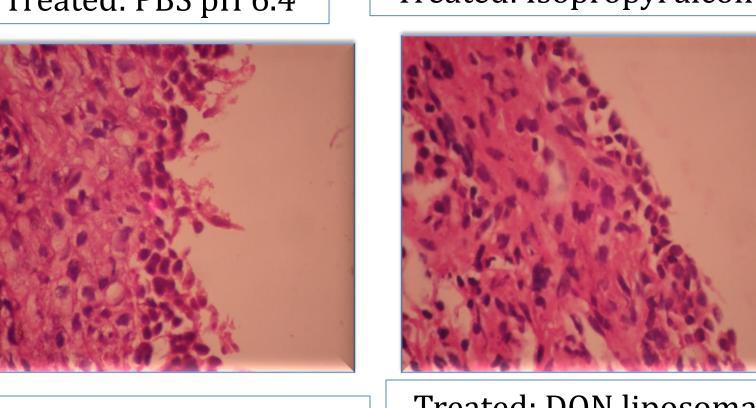
#### NASAL CILIOTOXICITY STUDY

300

Ammonium sulphate concentration (mM)

250





Treated: Blank in-situ gel

80

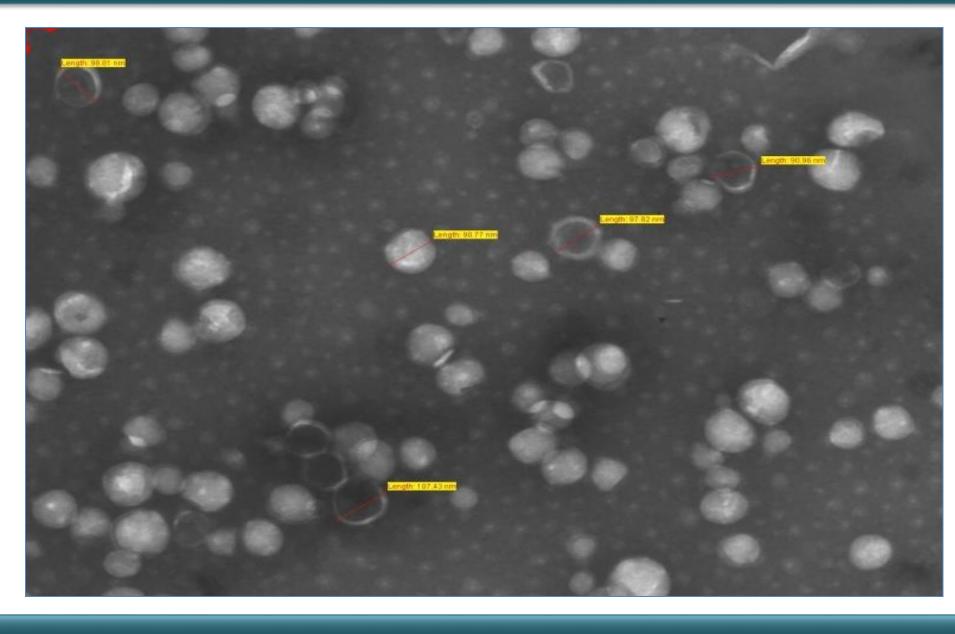
20

Treated: DON liposomal based gel

## CONCLUSION

- To develop a brain-specific Donepezil liposomes, we designed novel liposomes with cholesterol and phosphotidylcholine (HSPC) hydrogenated soya brain delivery.
- The liposomal system is having particles of a size 110 nm with entrapment efficiency of 90 %.
- The Donepezil liposomes was shown to be promising carriers due to the ability to load the compound, thus protecting the compound from degradation and in delivering the compound to the brain.
- DON liposome based in-situ gel showed 5.5 fold higher nasal permeation as compared to DON solution based gel.
- DON liposome based gel did not show toxicity and nasal mucosa was remained intact indicating its safety for intranasal administration
- In-vivo efficacy tested in scopolamine induced amnesia model indicated significant improvement in cognitive function in rats treated with developed liposomal based formulation as compared to the marketed tablet

## TEM OF DONEPEZIL LIPOSOME



## REFERENCES

- 1. Akbarzadeh A et al. Nanoscale Research Letters 2013, 8:102.
- 2. Abdulrahman KA et al. Drug Design, Development and Therapy. 2016; 10:205–15.