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FORMULATION AND EVALUATION OF FLOATING MICROSPHERES IN DONEPEZIL

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ABSTRACT

The study aims to formulate a novel retentive floating microsphere of Donepezil using different polymers (Ethylcellulose, Eudragit RS 100, HPMC K4M and Sodium CMC) by a solvent evaporation method. The floating microspheres were evaluated for percentage yield (%), particle size, drug content, drug entrapment efficiency, in-vitro floating ability and in-vitro drug release studies. The surface morphology of prepared microspheres was characterized by scanning electron microscopy. The microspheres were found to be spherical in shape and porous in nature. Compatibility studies were performed by fourier transform infrared (FTIR) technique. In-vitro release kinetics were studied in different release kinetics models like zero order, first order, higuchi and korsmeyer peppas model and the best fit model was found to be higuchi plot with release exponent n value less than 0.89. It was concluded that developed floating microspheres of donepezil offers a suitable and practical approach for prolonged release of drug over an extended period of time and thus oral bioavailability, efficacy and patient compliance is improved.

INTRODUCTION

Donepezil, also known as Aricept, is a piperidine derivative acetyl cholinesterase inhibitor used in the management of the dementia of Alzheimer's Disease, and in some cases, is used to manage other types of dementia. By inhibiting the acetyl cholinesterase enzyme, donepezil improves the cognitive and behavioral signs and symptoms of Alzheimer's Disease, which may include apathy, aggression, confusion, and psychosis. Donepezil is slowly absorbed via the gastrointestinal tract after oral administration.

Donepezil crosses the blood-brain barrier and cerebrospinal fluid concentrations at the above doses have been measured at 15.7%. Donepezil is 96% protein-bound, with approximately 75% binding to albumin and approximately 21% binding to alpha-1-glycoprotein. Signs and symptoms of overdose with cholinesterase inhibitors such as donepezil can include severe nausea and vomiting, bradycardia, hypotension, perspiration, seizures, muscle weakness respiratory depression.

METHODOLOGY:

Development of alignment bends of Donepezil in 0.1N HCL

Strategy: Working norm: 100mg of Donepezil was gauged and broken up in 10ml methanol and afterwards makeup to the volume with 0.1N HCl, it gives 1000µg/ml concentrated stock arrangement. Weakening 1: From the functioning norm, the 10ml arrangement was weakened to 100ml with 0.1N HCl, which will give 100 µg/ml concentrated arrangements. Weakening 2: From weakening 1, take 0.2, 0.4, 0.6, 0.8, and 1ml of arrangement was weakened sufficiently with 0.1N Hcl in 10ml volumetric carafe to acquire 2, 4, 6, 8 and 10µg/ml concentrated arrangements. This arrangements absorbance was noted at 353nm. **CHARACTERIZATION OF FLOATING MICROSPHERES:**

Particle Size Analysis: The particle size of floating microspheres varied somewhat among the formulation due to variation in the composition of formulations. The effects of stirring speed and polymer to polymer ratio on the particle size of microspheres are shown.

Percentage Yield:

Percentage Yield: The percentage yield was calculated using the f ollowing formula:

$$\% \text{ Yield} = \frac{\text{Practical mass (Floating microspheres)}}{\text{Theoretical mass (Polymer + Drug)}} \times 100$$

Drug entrapment efficiency: Floating microspheres equivalent to 4 mg of the drug Donepezil were taken for evaluation. The amount of drug entrapped was estimated by crushing the floating microspheres. The powder was transferred to a 100 ml volumetric flask and dissolved in 10ml of methanol and the volume was made up using 0.1N HCl. After 24 hours the solution was filtered through Whatman filter paper and the absorbance was measured after suitable dilution spectrophotometrically at 230 nm. The amount of drug entrapped in the floating microspheres

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{Experimental Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

***In-vitro* buoyancy study:** Microspheres (180 mg) were spread over the surface of a USP XXIV dissolution apparatus type II filled with 900 ml of 0.1N hydrochloric acid. The medium was agitated with a paddle rotating at 50 rpm for 12 h. The floating and the settled fractions of microspheres were recovered separately, dried and weighed. Buoyancy (%) was calculated as the ratio of the mass of the microspheres that remained floating to the total mass of the microspheres, expressed as a percentage.

RESULTS:

Construction of Standard calibration curve of Donepezil in 0.1N HCl: The absorbance of the solution was measured at 353nm, using a UV spectrometer with 0.1N Hcl as blank. The values are shown in the table. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10 µg/ml.

Inference: The bulk density and the tapped density for all formulations were found to be almost similar. Carr's index and Hausner's ratio were found to be in the range of ≤ 18 and 1.11 to 1.17 respectively, indicating good flow and compressibility of the blends. The angle of repose for all the formulations was found to be in the range of 31.75-37.83˚ which indicating passable flow.

EVALUATION AND CHARACTERISATION OF FLOATING MICROSPHERES

Particle Size Analysis: The particle size of floating microspheres varied somewhat among the formulation due to variation in the composition of formulations. The effects of stirring speed and polymer to polymer ratio on the particle size of microspheres are shown in the table4a.

FTIR STUDIES: The spectral data suggest that the major peaks for drugs are

obtained as nearer value and there were no considerable changes in IR peaks in all physical mixtures of drug and polymers. This indicates that the drugs were molecularly dispersed in the polymers or drug-loaded formulations thus thereby indicating the absence of any interactions.

Percentage Yield: The percentage yield was found to be in the range of 80 to 98% for floating Microspheres is recorded.

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Table 1: Formulation table for Donepezil

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
Donepezil	500	500	500	500	500	500	500	500	500
Ethyl Cellulose	200	300	400	200	300	400	200	300	400
Eudrigit RS100	300	200	100	--	--	--	--	--	--
HPMCK4M	--	--	--	300	200	100	--	--	--
Sodium CMC	--	--	--	--	--	--	300	200	100

Table 2: Standard Calibration graph values of Donepezil in 0.1N Hcl

Concentration(µg/ml)	Absorbance
0	0
2	0.182
4	0.369
6	0.541
8	0.735
10	0.919

Standard plot Donepezil plotted by taking absorbance on Y-axis and concentration (µg/ml) on X-axis, the plot is shown fig.

Table 3: Pre formulation studies

Formulation Code	Bulk density	Tapped density	Cars index	Hausner's ratio	Angle of repose
F1	0.54	0.61	11.47	1.12	31.26
F2	0.52	0.59	11.86	1.13	32.31
F3	0.45	0.50	10.00	1.11	30.42
F4	0.44	0.51	13.72	1.15	33.81
F5	0.4	0.45	11.11	1.12	32.14
F6	0.48	0.55	12.72	1.14	34.38
F7	0.50	0.56	10.71	1.12	31.75
F8	0.45	0.53	15.09	1.17	37.83
F9	0.4	0.45	11.11	1.12	32.14

Table 4(a): Results for Particle size

Formulation code	Particle size (µm)
F1	238.38
F2	328.47
F3	368.49
F4	271.12
F5	326.49
F6	336.33
F7	255.81
F8	292.62
F9	382.21

Table 4(b): Results for % Yield

Formulation code	% yield
F1	83.16
F2	95.67
F3	97.89
F4	87.99
F5	93.12
F6	94.67
F7	88.26
F8	82.85
F9	86.28

Table 4(c): Results for % Drug entrapment efficiency

Formulation code	% Drug entrapment efficiency
F1	67.86± 0.15
F2	91.20± 0.08
F3	70.33± 0.052
F4	85.80± 0.42
F5	82.93± 0.75
F6	89.37± 0.012
F7	74.26± 0.085
F8	77.13± 0.45
F9	86.67± 0.45

Table 4(d): Results for *In-vitro* buoyancy

Formulation code	In-vitro buoyancy
F1	83
F2	91
F3	97
F4	73
F5	78
F6	87
F7	71
F8	84
F9	74

Table 4(e): *In-Vitro* drug release data of Donepezil floating Microspheres

Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	29	23	11	32	26	21	22	16	9
2	53	39	19	57	42	38	39	29	15
4	85	55	34	79	69	55	55	43	25
6	99	73	53	98	82	74	71	60	42
8		99	75		99	87	87	76	58
10			91			99	99	84	73
12			98					93	85

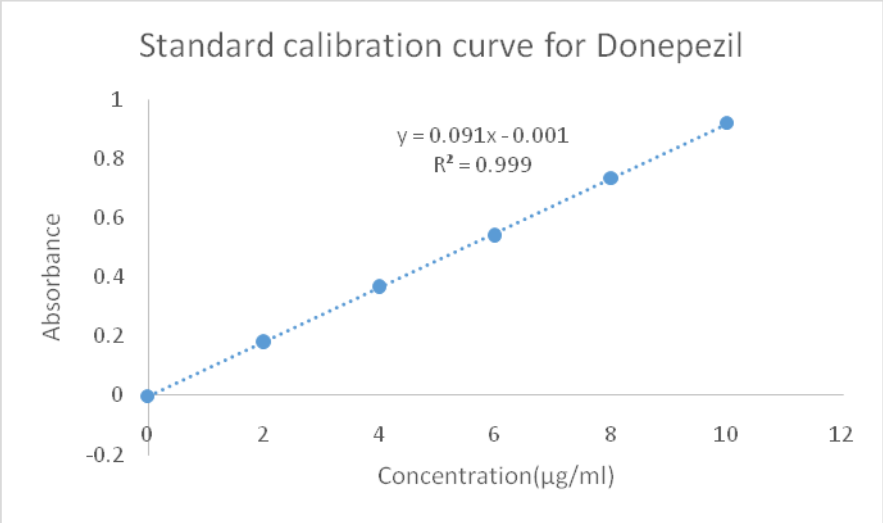

Fig.1: Standard calibration curve of Donepezil in 0.1N HCl

Inference: The standard calibration curve of Donepezil in 0.1N Hcl showed a good correlatio

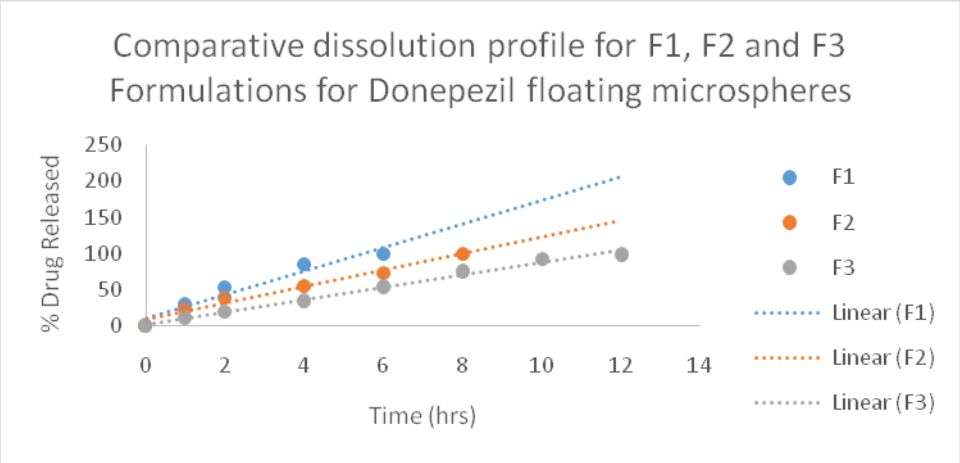

Fig.2(a): Comparative dissolution profile for F1, F2 and F3 formulations for Donepezil floating microspheres

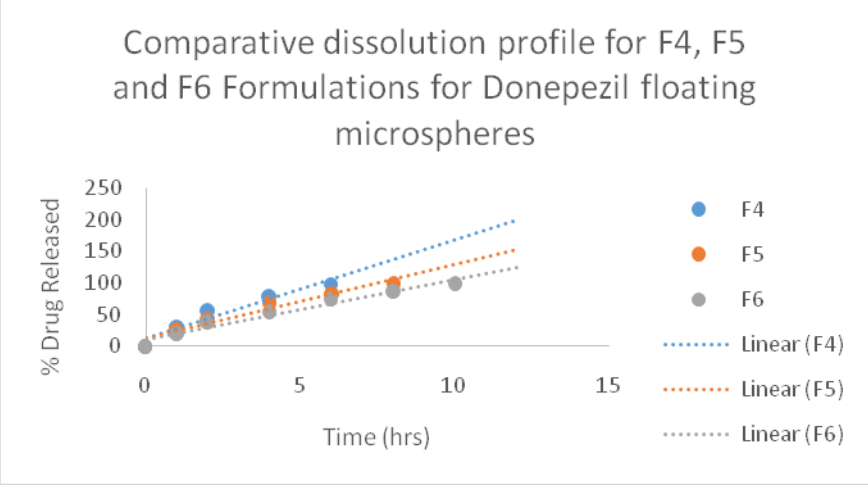

Fig.2(b): Comparative dissolution profile for F4, F5 and F6 formulations for Donepezil floating microspheres

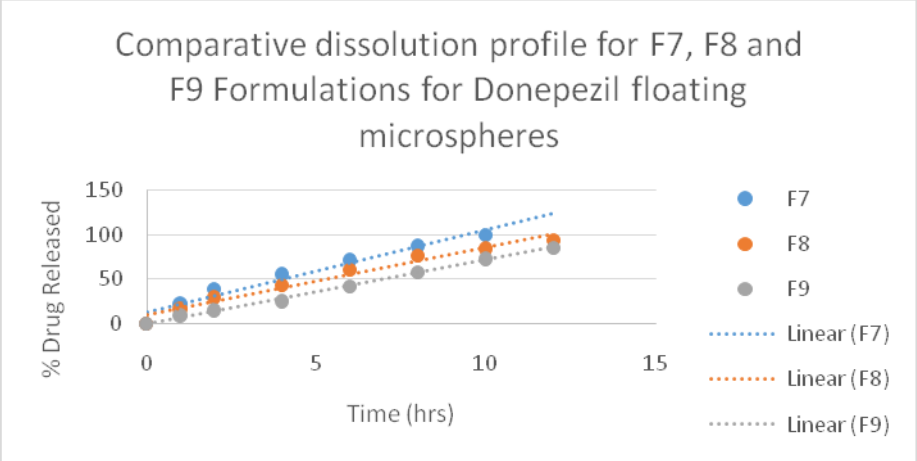

Fig.2(c): Comparative dissolution profile for F7, F8 and F9 formulations for Donepezil floating microspheres

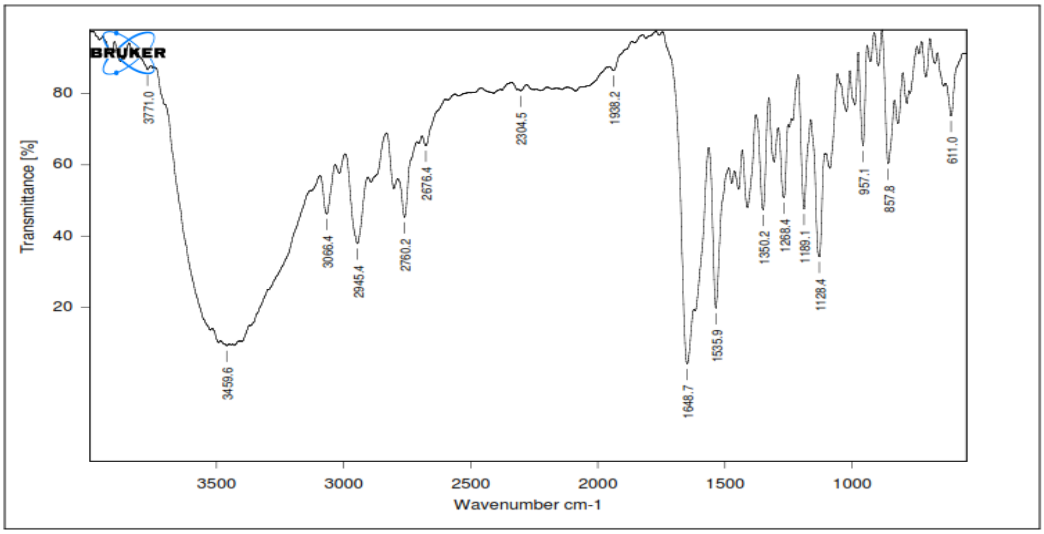

Fig. 3 : FTIR graph for Donepezil

CONCLUSION

In the present work, floating microspheres of Donepezil using Ethylcellulose, Eudragit RS100, HPMC K4M and Sodium CMC as copolymers were formulated to deliver Donepezil via the oral route. The *in-vitro* drug release decreased with an increase in the polymer concentration. Based on the results of evaluation tests form ulation coded F3 was concluded as the best formulation.

BIBLIOGRAPHY

1. Brahmankar DM., Jaiswal SB., Biopharmaceutics and Pharmacokine tics A Treatise, First Edition, Vallabh Prakashan, 1995, 337.

2. Chien YW; Rate-controlled Drug Delivery Systems; Indian J Pharm Sci, 1988; 63-65.

3. Brahmankar DM, Jaiswal SB, Biopharmaceutics and Pharmacokinetics A Treatise, First edition, Vallabh Prakashan, 2001, 337-341.

4. Baumgartner, Kristal J, Veer F, Vodopivec P and Zorko B; Optimisation of Floating matrix tablet and evaluation of their gastric residence time; Int J Pharm, 195, 2000, 125 – 130.

5. Machine.E. Bhandke; Formulation and Development of Repaglinide Microparticles by Ionotropic Gelation Techniques; Indian J Pharm Edu Res, 2006.

6. Rouge N, Buri P, Voelker E; Drug absorption sites in the gastrointestinal tract and Dosage forms for site-specific delivery; Int J Pharm, 136, 1996,117-139.

7. Thomas Wai-Yip Lee and Joseph R. Robinson, Controlled Release Drug-Delivery Systems, Chapter 47, Remington's Pharmaceutical Sciences, 20th Edition, Mack Publishing Company, Volume-I, 2000, 903-929.

8. Gohel MC, Amin AF; Formulation optimization of controlled release diclofenac sodium microspheres using factorial design; J Control Release, 51, 1998, 115-122.

9. Vase JK, Tambwekar K, Garg S; Bioadhesive microspheres as a controlled drug delivery system; Int J Pharm,255, 2003,13-32.

10. Ikeda K, Murata K, Kobayashi M and Noda K; Enhancement of bioavailability of dopamine via the nasal route in beagle dogs; Chem Pharm Bull (Tokyo),40, 1992, 2155-2158.

11. Nagai T, Nishimoto Y, Nambu N, Suzuki Y, Sekine K; Powder dosage form of insulin for nasal administration; J Control Release, 1, 1984, 15-22.

12. Ilium L, Farraj NF, Critchley H, Davis SS; Nasal administration of gentamicin using a Novel microsphere delivery system; Int J Pharm, 46, 1988, 261-265.