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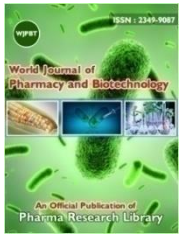

Formulation and *In-vitro* Evaluation of Rivastigmine Transdermal Patches

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A B S T R A C T

Rivastigmine is a acetylcholinesterase inhibitor used for the treatment of mild to moderate Alzheimer's disease and Parkinson's. In present study transdermal drug delivery of Rivastigmine was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Oral drug delivery system has various drawbacks like poor bioavailability due to hepatic metabolism (first pass) and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high and/or frequent dosing, which can be both cost prohibitive and inconvenient. Matrix type of transdermal patches was developed by using Guar gum (mg), Carrageenan gum (mg), Eudragit L 100 Transdermal patches were prepared by employing solvent casting method. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1-F9, and all the formulations were evaluated for various physical parameters Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake, Moisture content and Swelling study and all the results were found to be were found to be with in the pharmacopeial limits, in-vitro drug release studies by using dialysis membrane. Among all the 9 formulations F6 formulation which contain Carrageenan gum 40mg had shown 98.43% cumulative drug release within 12 hours.

Keywords: Rivastigmine, Transdermal patch, Guar gum (mg), Carrageenan gum (mg), Eudragit L 100

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C O N T E N T S

1. Introduction

The conventional treatments for the management of Alizemers Disease have all been administered orally. Some of the adverse effects of cholinesterase inhibitors, such as donepezil, galantamine, physostigmine, tacrine, phencerine and Rivastigmine that occur and often lead to termination of treatment by patients, are hepatotoxicity, renal failure and asthenia or malaise. Transdermal therapy has the potential to decrease the side effects of oral administration of drugs and providing easier access to optimal doses, benefits which would improve patient compliance. Rivastigmine is a reversible cholinesterase (acetylcholinesterase and butyrylcholinesterase) inhibitor for the treatment of mild to moderate alzheimer disease.

2. Materials and Methods

Materials: Rivastigmine, Eudragit L-100, Guar gum, Carrageenan gum, Ethanol, Dimethylformamide, Propylene glycol all the chemicals used were laboratory grade.

Method of Preparation:

Transdermal patches were prepared according to the formula shown in Table 1. Eudragit L100, Guar gum, Carrageenan gum were weighed in requisite ratios and they were then dissolved in dimethyl formamide and ethanol as solvent using magnetic stirrer. Rivastigmine (40mg) with a magnetic stirrer. Propylene glycol was added to the above dispersion under continuous stirring. The uniform dispersion was poured in the petri plate. The rate of evaporation of solvent was controlled by inverting cut funnel over the patches. After 24h, the dried patches were taken out and stored in desiccator.

Evaluation of post compression parameters for prepared Tablets:

The designed patches were studied for their physicochemical properties like Physical appearance, weight variation, Flatness, thickness, Folding endurance, Moisture uptake, Moisture content , Drug content determination and In vitro permeation studies using dialysis membrane.

3. Results and Discussion

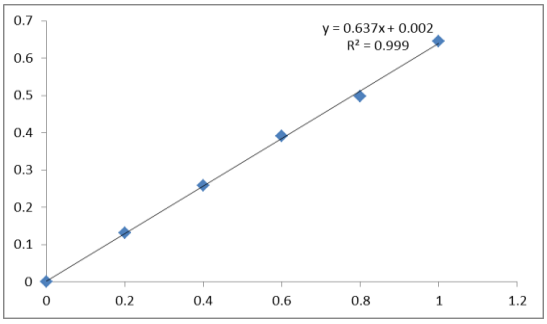

Fig 1: Standard curve of Rivastigmine

Evaluation of Rivastigmine Transdermal patches :

Physical appearance : All the Transdermal patches were visually inspected for colour, clarity, flexibility.

Flatness: All the Transdermal patches was found to be flat without any foams. The prepared Rivastigmine Transdermal patches were evaluated for their physical parameters such as Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake, Moisture content and all the results were found to be were found to be with in the pharmacopeial limits.

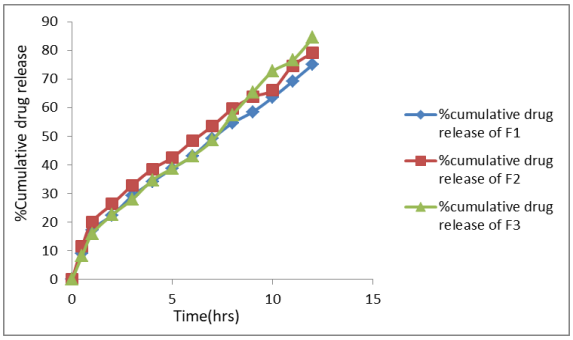

Fig 2:% drug release of F1, F2, F3

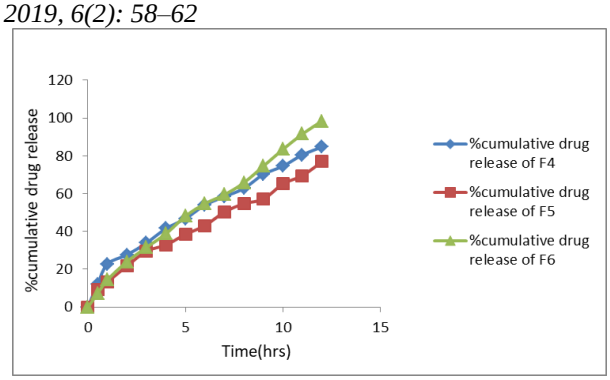

Fig 3:% drug release of F4, F5, F6

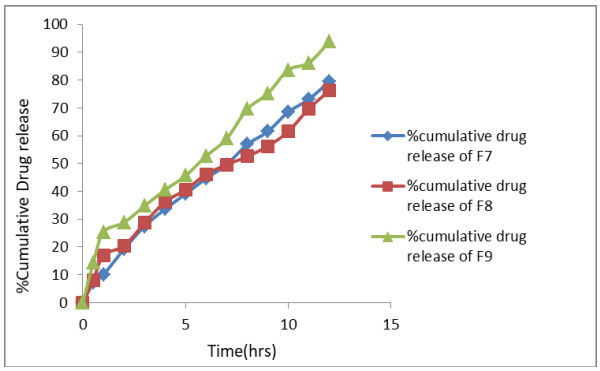

Fig 4:% drug release of F7, F8, F9

The prepared Rivastigmine Transdermal patches were evaluated for In-vitro permeation studies using dialysis membrane, among all the 9 formulations F6 formulation was shown 98.43% cumulative drug release within 12 hours.

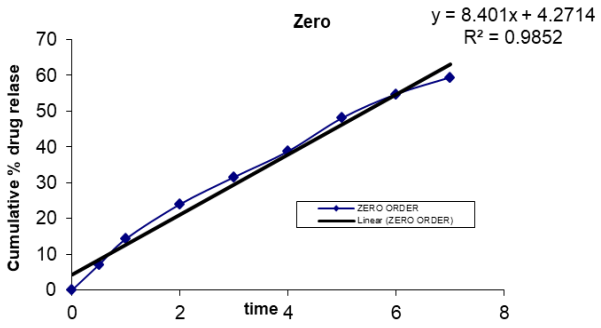

Fig 5: Zero order release kinetics graph

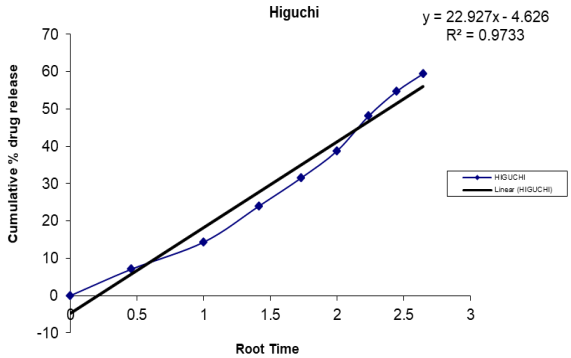

Fig 6: Higuchi release kinetics graph

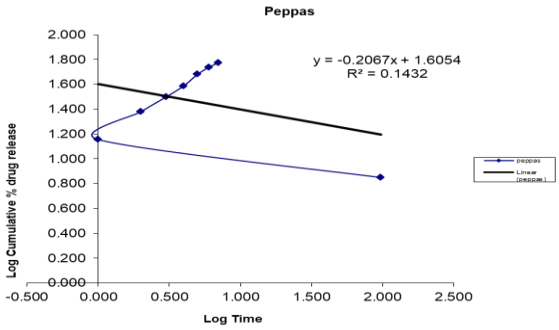

Fig 7: Kars mayer peppas graph

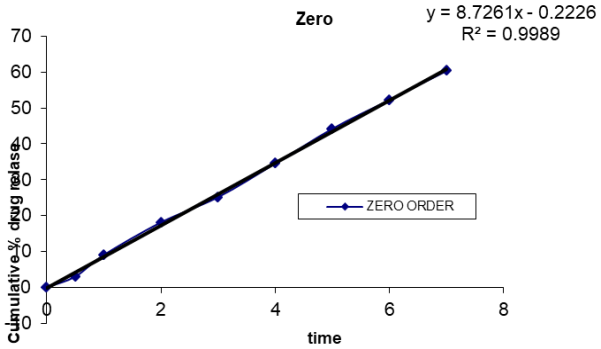

Fig 6: Zero order release kinetics graph

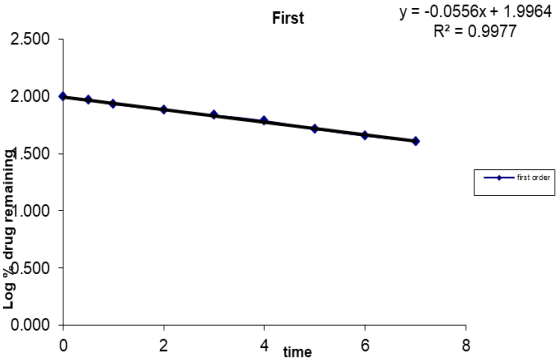

Fig 8: First order release kinetics graph

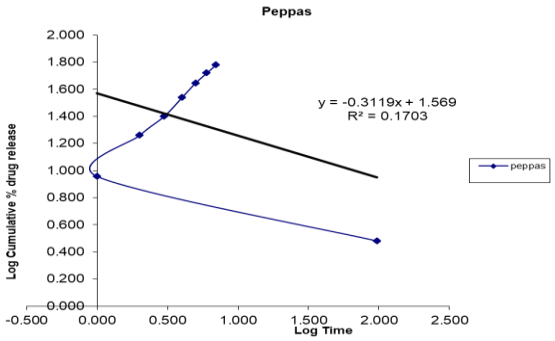

Fig 7: Higuchi release kinetics graph

Table 1: Formulations of Rivastigmine Transdermal Patches

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Drug(mg)	40	40	40	40	40	40	40	40	40
2	Guar gum (mg)	20	30	40	-	-	-	-	-	-
3	Carrageenan gum (mg)	-	-	-	20	30	40	-	-	-
4	Eudragit L 100	-	-	-	-	-	-	20	30	40
5	Dimethyl formamide (ml)	10	10	10	10	10	10	10	10	10
6	Ethanol(ml)	5	5	5	5	5	5	5	5	5
7	Propylene glycol(Drops)	5	5	5	5	5	5	5	5	5

Table 2: Standard graph of Rivastigmine

Concentration (µg/ml)	Absorbance
0	0
0.2	0.131
0.4	0.258
0.6	0.391
0.8	0.498
1	0.645

Table 3: Evaluation of Rivastigmine Transdermal patch by physical methods

Formulation	Weight variation (mg)	Thickness (mm)	Folding endurance	Drug content (%)	Moisture uptake (%)	Moisture content (%)
F1	102	0.104	178	98.09	1.98	2.15
F2	99	0.121	181	97.65	1.87	2.18
F3	98	0.131	178	99.08	2.08	1.56
F4	99	0.128	189	98.54	2.19	1.92
F5	93	0.125	190	99.43	2.43	1.82
F6	98	0.129	191	98.06	1.28	2.75
F7	96	0.124	198	99.32	2.05	2.09
F8	100	0.125	199	97.51	1.19	1.32
F9	102	0.109	195	98.09	1.28	2.19

Table 4: Evaluation of Rivastigmine Transdermal patch by In-vitro permeation studies using dialysis membrane

Time (Hrs)	% Drug release								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
0.5	9.03	11.45	8.34	12.09	9.21	7.08	7.11	8.09	14.27
1	17.24	20.09	15.87	22.78	13.24	14.32	10.12	16.99	25.37
2	22.39	26.31	22.58	27.61	21.67	23.98	19.23	20.46	28.82
3	29.13	32.87	27.92	33.89	29.54	31.54	27.45	28.64	34.77
4	34.12	38.53	34.65	41.52	32.85	38.76	33.65	36.23	40.54
5	38.76	42.56	38.79	46.78	38.45	48.06	39.09	40.57	45.63
6	43.07	48.30	43.07	53.97	43.09	54.72	44.67	46.18	52.72
7	49.21	53.62	48.56	58.42	50.24	59.41	49.65	49.60	58.92
8	54.62	59.63	57.43	62.78	54.73	65.83	56.87	52.54	69.53
9	58.47	63.75	65.27	70.23	57.12	74.56	61.53	56.27	75.15
10	63.52	66.20	72.69	74.56	65.18	83.45	68.53	61.54	83.63
11	69.19	74.65	76.54	80.54	69.54	91.56	73.09	69.72	86.19
12	75.04	79.08	84.43	84.67	76.98	98.43	79.54	76.17	93.87

Table 5: Release kinetics data for optimized formulation

Cumulative (%) Release Q	Time (T)	Root (T)	LOG(%) Release	LOG (T)	LOG (%) Remain
0	**0**	0			2.000
7.08	0.5	0.458	0.850	1.987	1.968
14.32	1	1.000	1.156	0.000	1.933
23.98	**2**	1.414	1.380	0.301	1.881
31.54	**3**	1.732	1.499	0.477	1.835
38.76	**4**	2.000	1.588	0.602	1.787
48.06	**5**	2.236	1.682	0.699	1.716
54.72	**6**	2.449	1.738	0.778	1.656
59.41	**7**	2.646	1.774	0.845	1.608
65.83	**8**	2.828	1.818	0.903	1.534
74.56	**9**	3.000	1.873	0.954	1.406
83.45	**10**	3.162	1.921	1.000	1.219
91.56	**11**	3.317	1.962	1.041	0.926
98.43	**12**	3.317	1.821	1.350	1.162

4. Conclusion

In present study transdermal drug delivery of Rivastigmine was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Oral drug delivery system has various drawbacks like poor bioavailability due to hepatic metabolism (first pass) and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high and/or frequent dosing, which can be both cost prohibitive and inconvenient. Matrix type of transdermal patches was developed by using Guar gum (mg), Carrageenan gum (mg), Eudragit L 100Transdermal patches were prepared by employing solvent casting method. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1-F9, and all the formulations were evaluated for various physical parameters Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake, Moisture content and Swelling study and all the results were found to be were found to be with in the pharmacopeial limits, invitro drug release studies by using dialysis membrane. Among all the 9 formulations F6 formulation which contain Carrageenan gum 40mg had shown 98.43% cumulative drug release within 12 hours.

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