ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

FORMULATION AND EVALUATION OF MEMANTINE ORAL FILMS

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ARTICLE INFO

Key words:
Memantine , Oral films, Formulation, Evaluation, HPMC

Access this article online
Website: https://www.jgtps.com/
Quick Response Code:

ABSTRACT

The aim of this present research work is to formulate and evaluate dissolving films using Memantine hydrochloride as a model drug which is used for facilitating rapid onset of action in Alzheimer's patients who are mentally ill. The films were designed to dissolve upon contact with a wet surface, such as tongue, within a few seconds especially for these patients who are unable to swallow. In this present research work various trials were carried out using different grades of HPMC E5, E15 and E15CPS by solvent casting method. The prepared films were eva1uated for morphological properties, weight variation, drug content uniformity, thickness uniformity, folding endurance, surface pH, In-vitro disintegration time, *In-vitro* dissolution studies and stability studies of the satisfactory formulation. Memantine orally disintegrating films were successfully prepared with HPMC E15CPS and HPMC E15 & HPMC E5 combination. These findings suggest that the fast dissolving film containing Memantine is considered to be potentially useful for the treatment of Alzheimer's where geriatric patients feel difficulty to swallow a dosage form.

INTRODUCTION

Memantine is used to treat the symptoms of Alzheimer's disease (AD; a brain disease that slowly destroys the memory and the ability to think, learn, communicate and handle daily activities). Memantine is in a class of medications called NMDA receptor antagonists. It works by decreasing abnormal activity in the brain. Common side effects include headache, constipation, sleepiness, and dizziness. Severe side effects may include blood clots, psychosis, and heart failure.

MATERIALS AND METHOD

Analytical Method Development Readiness of 6.8 phosphate cradle: 6.8gms of potassium dihydrogen orthophosphate was taken in a 1000ml volumetric jar andbroke down with refined water and makeup to 1000 ml with refined water and change pH up to 6.8with Sodium hydroxide arrangement. Assurance of λmax of Memantine in 6.8 phosphate support:

Solvency assurance: The solvency of medication was controlled by immersion dissolvability strategy. In this, an abundance measure of medication was added to 25ml of water and set on a gyratory shaker for 24hr. Then, at that point arrangement was sifted and weakened with water. the absorbance of this example was found by UV-spectrophotometer and results are deciphered as far as solvency.

Formulation of Memantine quick-dissolving films: The mouth dissolving film of Memantine was ready by the dissolvable projecting procedure. Arrangement 'A' was ready by dissolving HPMC-E15 polymer in 5 ml of water. Arrangement 'B' was ready by

dissolving Memantine, Aspartame, Sorbitol and citrus extract in 5 ml of ethanol. The arrangements 'A' and 'B' were blended and mixed for 30min. also, add Propylene glycol and tween 80 and enhancing specialist and keep blending for 10mins. The arrangements were projected on to glass Petri plate of 9 cm distance across and were dried in the broiler at 70°C till a peelable film was shaped. Then, at that point, dried movies were cut into rectangular shape pieces, with a 4.0 cm2 (2.0 cm × 2.0 cm) complete surface region. The wanted amount of Memantine was 10 mg (a portion of medication) per 4.0 cm2 films.

Evaluation of orally disintegrating films

1. Weight uniformity
2. Morphological properties
3. Thickness uniformity
4. Folding endurance
5. Surface pH
6. Drug content uniformity test
7. In-vitro disintegration test
8. In-vitro dissolution studies

Morphological properties

This parameter was checked simply with visual inspection for the physical appearance of films and evaluation of texture by feel or touch.

Thickness uniformity

All eight batches were evaluated for thickness by using calibrated Vernier calliper with a least count of 0.01mm. The thickness was measured at three different spots of the films and the average was taken.

Weight uniformity of films

Three films of each formulation trial of 2cm*2cm size were taken and weighed individually in electronic balance and the average weights were calculated. The number of times the film could be folded at the same place without breaking gave the value of folding endurance.

Surface pH: Surface pH was found out by placing the film on the surface of 1ml of distilled water. The surface pH was noted by bringing pH paper near the surface of the films and allowing it to equilibrate for 1min. The change in the colour of pH paper was observed.

Uniformity test: For this, each strip at three different places equivalent to 2mg of drug was cut and dissolved in 50ml of 6.8 Ph phosphate buffer solution with continuous stirring. This solution was filtered using Whatman filter paper, and the filtrate was diluted to 100ml with the same buffer in a volumetric flask. This solution was analyzed by U.V. Spectrophotometer and the absorbance was recorded at 280nm. Drug content was calculated by using the calibration curve of the drug.

***In-vitro* disintegration test:**

In-vitro disintegration time is determined visually in a glass dish of 25ml distilled water with swirling every 10 sec. The disintegration time is the time when the film starts to break or disintegrates.

***In vitro* dissolution studies**

The in vitro dissolution test was performed in a Ph. Eur. 6.4 Ed. Paddle dissolution apparatus. The dissolution medium consisted of 900 mL 6.8pH phosphate buffer solution, 37±0.5°C and stirred at 50 rpm. Drug release was analyzed spectrophotometrically at 280nm.

RESULTS AND DISCUSSION

Stability studies of physical and chemical parameters: Selected formulation F4 was strip packed and stored at 40°C ± 2°C / 75% ± 5% RH or a period of 1 month. Samples were analyzed after storage for 1month and evaluated

Table 1: Construction of Standard calibration curve of Memantine in 6.8 phosphate buffer

Concentration (µg / ml)	Absorbance
0	0
5	0.133
10	0.255
15	0.382
20	0.49
25	0.611

Standard plot of Memantine plotted by taking absorbance on Y – axis and concentration(µg/ml) on X – axis.

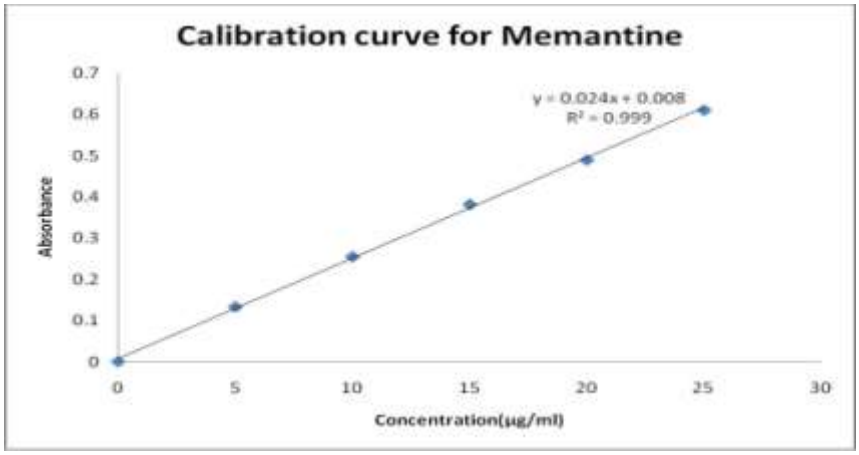

Fig. 1: Calibration curve of Memantine

Table 2: Results of formulation

Formulation code	*Appearance*	*Thickness (mm)*	*Weight variation*	*Folding endurance*	*% Assay*	*Dintegration time(sec)*
F1	*Smooth and Transparent*	*0.234*	*87*	*42*	*99.13*	*19*
F2	*Smooth and Transparent*	*0.271*	*91*	*51*	*98.79*	*24*
F3	*Smooth and Transparent*	*0.263*	*83*	*38*	*99.82*	*21*
F4	*Smooth and Transparent*	*0.247*	*85*	*57*	*100.17*	*27*
F5	*Smooth and Transparent*	*0.257*	*87*	*54*	*99.48*	*32*
F6	*Smooth and Transparent*	*0.234*	*90*	*49*	*101.07*	*28*

Table 3: Results of percent drug release

TIME (min)	**% DRUG RELEASE**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	**0**
3	24	23	35	27	26	24	39	63	**65**
6	31	35	46	35	39	31	61	76	**86**
9	38	41	58	49	51	53	83	83	**95**
12	53	50	72	63	68	68	97	95	**100**
15	64	59	79	75	80	81	98	99	
18	71	70	85	86	89	95	98		
21	78	82	92	97	97	99			
24	82	89	99	99	100				
27	85	94							
30	91	97							

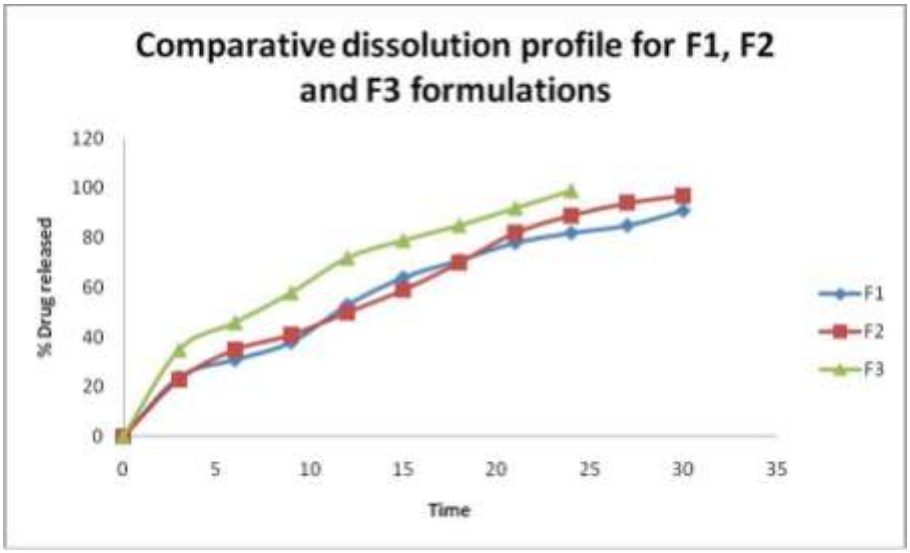

Fig. 2: Results of Dissolution profile for F1, F2, F3

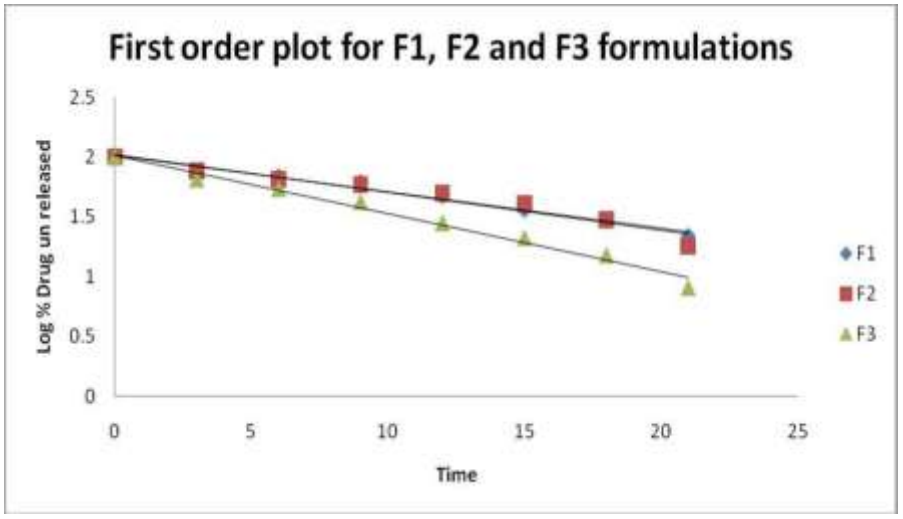

Fig. 3: Results of first order plot for F1, F2, F3

Table 4: Results of zero and first order

Formulation code	Zero order	First order
F9	0.789	0.999

Table 5: Results of stability studies

TIME	Initial	1 Month
0	**0**	0
3	**65**	64
6	**86**	87
9	**95**	95
12	**100**	100

SUMMARY &CONCLUSION

1. Memantine orally disintegrating films were successfully prepared with HPMCE15CPS and HPMC E15 & HPMC E5 combination.
2. Thicknesses were in the range of 0.234 mm to 0.271mm.
3. The weights of the films were found to be in the range of ±10%.

4. Folding endurance of the films was found to be in the range of 38± 1 to 57 ± 2.
5. The surface pHs of all the films were found to be neutral as there was no colour
6. Change in the litmus paper. 6. The drug content uniformity is performed by taking three films in each formulation trial and the average drug content was calculated. And all the films were found to be 98 to 10.2.
7. The disintegration time of the prepared films
8. Acceptable mechanical properties were obtains and disintegration time was below 27 sec
9. It was concluded that formulations F-9 were optimised for the desirable properties

CONFLICT OF INTEREST

The authors declare no conflict of interest

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