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Development of Formulation and Assessment of Memantine Hydrochloride orally Tablets

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ARTICLE DETAILS

Research Paper

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ABSTRACT

The main objective of the present investigation was to develop a method for quantifying the amount of Memantine Hydrochloride present in tablets that are easily ingested and administered. This was achieved through the use of a dry granulation process. The F5 formulation yielded good results when the dry granulation process was used with Microcrystalline Cellulose PH 102 and Anhydrous Lactose. In addition to other medicinal attributes, the generated tablet formulations were evaluated for friability (%), thickness, hardness, and disintegration time. It was discovered that % In-vitro Dissolution was reported to be 99.87%, and % drug content was found to be 99.93%.

1. Introduction

The compound known as memantine is the earliest illustration in Fig. 1. 3,5-dimethyadamantan-1-amine;hydrochloride. Bears the molecular weight of 215.765g/mol and the chemical formula C12H21N.HCl. It is the first medication to receive approval from the United States Food and Drug Administration, and it is manufactured by Forest Pharmaceuticals under the brand name Namenda (1).

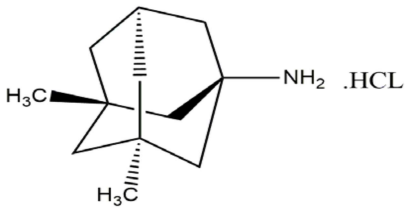

Fig. 1. Memantine hydrochloride's structure

This treatment has helped Alzheimer's patients with memory loss, confusion, and reasoning issues. By targeting the 5-HT3 receptor and inhibiting the glutamatergic NMDA receptor, this drug reduces nausea and causes cognitive problems. Memantine hydrochloride, an N-Methyl-D-Aspartase receptor antagonist, treats Alzheimer's disease. Memantine HCl, a biopharmaceutical class I molecule with logP = 3.28 and pKa = 10, is extremely permeable and soluble (35 mg/ml in water at 20◦C) (3). Dementia impairs memory, reasoning, orientation, comprehension, computation, learning, language, and judgement. Most frequent form of dementia, Alzheimer's disease, causes 11.9% of non-communicable illness-related disability years. It's the leading cause of old age impairment. Memory deficits usually occur early in the illness and might hinder daily tasks and work. The amnesia with this illness is severe and worsens with age. Familial Alzheimer's disease, which affects 5–10% of cases, is rare. A dominant gene passed down from generation to generation causes it. The sporadic variety accounts for 90% of cases and can occur in families without a history of the illness (4).

2. MATERIALS AND METHODS

Materials

Memantine Hydrochloride **was obtained as kind gift Sample from Akums drugs and Pharmaceutical Limited Haridwar,.** Microcrystalline Cellulose PH102, Anhydrous Lactose**,** Starch, Mannital**,** Sodium starch glycolate, Talk, and Magnesium Stearate **were obtained as kind gift Sample from Alkem Laboratories Mumbai,. All the materials were used as an analytical grade.**

Methods

a) Memantine's Standard Curve (7)

Phosphate buffer pH 6.8 was used to generate a Memantine standard calibration curve, having a wavelength of 229 nm for λMax.

b) Estimating the Blend before Compression (4)

Using a 25 g weighted volume of blend in a 100 ml measuring cylinder, the characterisation study comprises assessing the bulk and tapped densities, Hausner ratio, angle of repose, Compressibility Index, and blend characteristics before compression.

Making tablets containing 5 mg of Memantine Hydrochloride (4)

Tablets containing 5 mg of memantine hydrochloride were made via dry granulation (F5).

Table No.1: Preparation of Tablet Content

Sr. No.	Ingredients	Formulation (mg) F1	Formulation (mg) F2	Formulation (mg) F3	Formulation (mg) F4	Formulation (mg) F5
1	Memantine Hydrochloride	5.00	5.00	5.00	5.00	5.00
2	Microcrystalline Cellulose PH102	5.00	58.50	58.00	60.00	58.00
3	Anhydrous Lactose	2.00	58.00	2.00	6.00	57.00
4	Starch	58.00	5.00	60.00	57.00	6.00
5	Mannital	60.00	3.00	5.00	2.00	2.00
6	Sodium starch glycolate	1.00	1.50	1.00	1.00	3.00
7	Colloidal Silicon Dioxide	0.60	0.60	0.60	0.60	0.60
8	Purified Talc	2.00	2.00	2.00	2.00	2.00
9	Magnesium Stearate	1.40	1.40	1.40	1.40	1.40
TOTAL		135.00	135.00	135.00	135.00	135.00

Dry granulation methodology

A maximum relative humidity of 65% and a maximum temperature of 30°C were used during the production process.

Step I: Given material Memantine Hydrochloride, Microcrystalline Cellulose PH102, Anhydrous Lactose, Starch, Mannital, Sodium starch glycolate, Colloidal Silicon Dioxide and Purified talc shifting were done using a 40 mesh size. Independently shift Magnesium Stearate using a 60 mesh size while maintaining a separate position.

Step II: Dry mix of Memantine Hydrochloride, Microcrystalline Cellulose PH102, Anhydrous Lactose, Starch, Mannital, Sodium starch glycolate, Colloidal Silicon Dioxide and Talc and it should be blended for a duration of 25 minutes.

Step III: Sifted Magnesium Stearate in step II and blend for 4 minutes.

Step IV: The lubricated blend was moved for compression.

Step V: Utilized was an 7.0 mm, upper punch and lower Punch plain, round standard concave punch was used. The in-process parameter for the standard weight is 135.0 mg. The individual weight variation is 135.0 mg with a tolerance of ±7.5%. The weight variation of 20 tablets is 2.700g with a tolerance of ±5%. The thickness should be 3.6±0.3mm. The hardness should be 5.5±3Kp. The friability should not exceed 1.0%. The disintegration time should not exceed 15 minutes. Description- Round, biconvex, white to off-white, uncoated tablet with plain on both sides.

Tablet characteristics after compression (5)(6)

Thickness and Diameter in-process parameter: The diameter and thickness of the tablets were measured with Vernier callipers.

Weight uniformity in-process parameter : After random selection, all twenty tablets were weighed to assess weight variance.

Weight Variation in-process parameter. The weight of the product's 20 tablets was calculated, taking into account the upper and lower limits.

Friability in-process parameter: The Electrolab Friabilator was used to assess the tablets' friability. This number is expressed as a percentage. The friabilator was used to weigh ten tablets. Three minutes were spent operating the friabilator at a pace of twenty-five revolutions per minute. Once the four minutes had passed, we took another look at the tablet weights. Then, the friability was determined using the following equation.

$$\text{Friability (\%)} = \frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \times 100$$

Hardness in-process parameter: Twenty tablets at random were measured for hardness using the Monsanto hardness tester.

Disintegration Time Test in-process parameter. The disintegration time of a tablet is measured with a disintegrator and water as the media, and it can only take up to 15 minutes to disintegrate completely.

c) Measuring Assay (4)

From each batch, thirty tablets were chosen at random. Ten of the thirty tablets were ground into a fine powder for the purpose. Before the powder was put through an assay test to confirm that it accurately reflected the label's claim, it was carefully metered and dissolved in the media.

d) Using Content Uniformity to Measure Solid Dosage Form Uniformity (4)

Initial steps consisted of swallowing a tablet, then adding 15 millilitres of methanol to a volumetric flask containing 100 milliliters, and then sonicating the mixture for ten minutes. Sonication was performed on the mixture for a period of fifteen minutes after 15 milliliters of 0.2 N sodium hydroxide solution was added and the mixture was shaken. Layer separation was accomplished by adding a 10 milliliter internal standard solution and stirring it gently for a period of fifteen minutes. This was done in order to achieve the desired results. A capillary pipette and anhydrous sodium Sulphate were utilized in order to separate and dry the toluene layer that was located the topmost. Two to three milliliters of the solution were separated, and the rest left for analysis.

e) Drug dissolution In-vitro (4)

A USP Type 2 paddle type apparatus was used for the in vitro dissolving test, and 900 ml of 0.01 N HCl were mixed at 37±0.5 °C and 50 rpm. At regular intervals of one, two, four, six, eight, and ten minutes, samples were taken.

3. RESULT AND DISCUSION

a) Memantine's standard curve

Table 1: The calibration graph values of memantine 6.8 phosphate buffer at λMax are 229 nm.

Concentration (µg/ml)	Absorbance
0	0
2	0.149
4	0.294
6	0.451
8	0.591
10	0.731

Fig. 1: Standard calibration curve of Memantine in 6.8 phosphate buffer

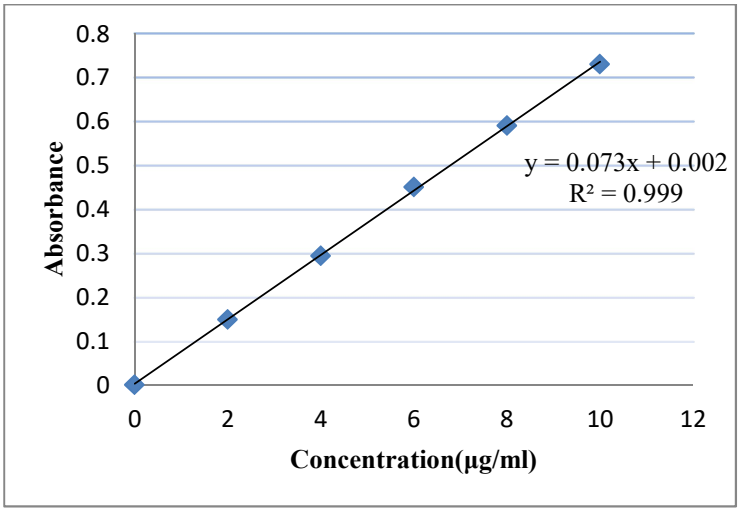

Fig. 2: Memantine's standard curve

Table 6: Assessment of Pre-compression Blend

Formulations	'Angle of repose' (degree± SD)	'Bulk Density' (g/mL± SD)	'Tapped Density' (g/mL± SD)	'Compressibility Index (%)' (%± SD)	'Hausner's ratio' (%± SD)
F1	24º.20±0.08	0.396±0.08	0.453±0.06	22.74±0.06	1.21±0.09
F2	23º.27±0.07	0.424±0.05	0.573±0.07	14.68±0.07	1.19±0.08
F3	26º.13±0.06	0.373±0.07	0.482±0.09	28.17±0.09	1.17±0.08
F4	25.29±0.08	0.408±0.04	0.523±0.07	13.55±0.05	1.13±0.05
F5	26º.31±0.05	0.481±0.06	0.563±0.04	11.94±0.07	1.12±0.07

Table 7: Assessment of uncoated tablets

Formulations	'Weight Variation' (mg)	'Hardness' (kg/cm^2)	'Thickness' (mm)	'Friability' (%)	'Disintegrating time' (minutes)
F1	136±1.26	5.35±0.71	3.61±0.21	0.16±0.09	7 min 44 Second
F2	138±0.69	5.50±0.46	3.62±0.41	0.24±0.12	9 min 30 Second
F3	135±0.68	5.60±0.53	3.61±0.11	0.14±0.13	6 min 31 Second
F4	134±0.94	4.80±0.32	3.65±0.21	0.21±0.09	7 min 56 Second
F5	**135±0.61**	**5.5±0.16**	**3.60±0.10**	**0.11±0.07**	**4 min 10 Second**

E) Estimating the Drug content

The drug concentration of the Memantine was found to be between 90.11 and 99.93; these values are within the allowed range.

Table No. 8: Estimating of % Drug

Formulation Code	%Drug content
F1	90.11
F2	93.52
F3	96.27
F4	98.79
F5	**99.93**

E) In vitro drug dissolution Investigations

Shown in Figure 3. The drug release in vitro was found to be 99.87%.

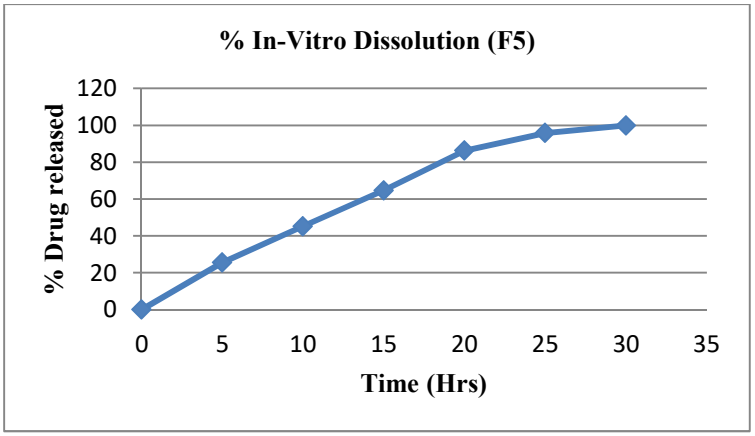

Fig.3: The invitro drug release profile of a manufactured tablet

4. CONCLUSION

Using the dry granulation process, 5 MG of Memantine Hydrochloride **tablets were created.** Microcrystalline Cellulose PH102, **and** Anhydrous Lactose **were utilised as the main diluents in formulation. The parameters of individual weight variation, hardness, thickness, friability, and disintegration time for** Memantine Hydrochloride **tablets were assessed and determined to be adequate. Drug content was found 99.93% and in-vitro dissolution found 99.87% of formulated tablets.**

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