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EFFECT OF HPMC VISCOSITY (TYPES) ON MEBEVERINE HCL 200MG TABLETS EXTENDED RELEASE

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ABSTRACT

In vitro release of Mebeverine HCl 200mg embedded in an extended release (ER) matrix, composed of various viscosity types of Hydroxy-propyl methylcellulose (HPMC), with Microcrystalline cellulose (MCC 102), Lactose anhydrous, Magnesium stearate, and Aerosil, was investigated, to study the effect of change of HPMC viscosity (5,15,50,4000, 10000, and 100000 mpas) in Mebeverine HCl release from tablet prepared by dry granulation method, release was studied for 13hrs, and release difference was clearly observed by changing HPMC viscosity.

KEYWORDS: Mebeverine HCl, Extended Rrelease, Hydrophilic Matrices, Hypermollose, Hydroxypropyl methylcellulose, HPMC, Dry granulation.

INTRODUCTION

Mebeverine hydrochloride is an antispasmodic with a direct action on the smooth muscle of the gastrointestinal tract. It is used in conditions such as irritable bowel syndrome (Sweetman, 2009). Hypermollose (Hydroxypropyl methyl cellulose, HPMC) matrices are widely used in hydrophilic extended release (ER) dosage forms , The objective of this study was a fundamental investigation of the effect of HPMC having various viscosities (5-100000cps) on release of Mebeverine HCl (very soluble material) from ER tablet.

MATERIAL

All materials were received as gift from Azal pharmaceutical co. Ltd./Sudan. All were pharmaceutical grade and within their expiry dates.

Mebeverine HCl (Rachempharma), HPMC E5 premium LV (Colorcon), HPMC HD15 (Shandong Head), HPMCE50 premium LV (Colorcon), HPMC HD4000CR(Shandong Head), HPMC K10M premium CR (Colorcon), HPMC K100M premium (Colorcon), Avecil 102(FMC biopolymer), Anhydrous Lactose (DFE pharma), Mg Stearate (Peter Greven), Colloidal Anhydrous Silica Aerosil (Evonic).

Experimental Methods

Preparation of tablets

Materials (Mebeverine HCL, HPMC, and anhydrous Lactose) were mixed well geometrically and designated as mixture A; Materials (Avecil 102,part of Aerosil, and part of Mg-Stearate) were mixed well then through mesh 850µm and designated as mixture B. These powder mixtures A and B were added together, mixed well, then passed throw mesh 850µm, then the final mixture was transferred to polyethylene bag and mixed manually for 5 minutes. This mixture was slugged by compression machine, grinded gently then passed through sieve 1 mm, The granules were Mixed with the rest of (Aerosil*, and Mg-Stearate*), passed again through sieve 1mm then mixed manually for 2 minutes in a polyethylene bag. Final mixture was compressed using specified (Round Punch and Die Size 11.15 mm) with the accurate weight of 418 mg per tablet. The in process control was carried out to ensure the reproducibility of the quality of tablets.

Characterization of matrix formulations

Description: 20 tablets were randomly taken, inspected visually, and described. They were undamaged, smooth, and of uniform colour.

(http://www.who.int/medicines/publications/pharmacopoeia/Tabs-GeneralMono-rev-final_31032011.pdf.)

Thickness in mm: 20 tablets were taken randomly and tested by the Digital Vernia callipers. The average of measured thickness results in mm, was calculated.

Diameter in mm: 20 tablets were taken randomly and tested by the digital vernia calliper, and the average was calculated.

Width in mm: 20 tablets were taken randomly and tested to measure the width in mm by digital vernia callipers, and the average was calculated.

Hardness in KP: 20 tablets were taken randomly and tested individually by using hardness tester, and the average was calculated (USP, 2010).

Friability test: 20 tablets were randomly taken and carefully dedusted prior to testing. The tablet sample was accurately weighed, and placed in the drum. The drum was rotated 100 times, then the tablets were removed and dedusted as before, and accurately weighed. A maximum loss of mass not greater than 1.0 percent is considered acceptable for most products (BP, 2013).

Average Weight (Weight uniformity): 20 tablets were weighed individually and the average mass was calculated; standard deviation and relative standard deviation were calculated. RSD should not exceed ±5.0%.

(http://apps.who.int/phint/en/p/docf/).

Dissolution Profile

Dissolution testing and assay method were carried out according to (BP, 2013).

Apparatus: Apparatus 2 (paddle type)

Medium temperature: 37°C±0.5

Speed: 50 RPM

Time: 13 Hrs

Wave length: 263 nm

The dissolution medium was 750ml 0.1N HCL, in the first 2 hrs, then 250 ml of buffer (0.2M solution of trisodium phosphate dodecahydrate R) equilibrated to 37°C±0.5, was added, adjusted with 2M HCl R or 2M sodium hydroxide R to pH 6.8, while the apparatus was operating.5ml samples were withdrawn by means of a syringe fitted with filter on the dissolution tester through the specified time (3, 5, 7, 9,11and 13 hrs) and their absorbance measured at 263nm. The aliquots withdrawn for analysis were replaced with equal volumes of fresh dissolution medium at 37°C.

The content of the amount dissolved was calculated taking 263 as the value of (1%, 1cm) at the maximum 263 nm. The assay method was carried out as described in (BP, 2013).

Assay: 20 tablets were weighed and powdered. A quantity of the powdered tablets containing 0.5 g of Mebeverine Hydrochloride with 100 mL of 0.1M hydrochloric acid was heated for 10 minutes on a water bath, shaking occasionally. Cooled, and sufficient 0.1M hydrochloric acid to produce 250 mL were added and filtered. To 10 mL of the filtrate sufficient 0.1M hydrochloric acid to produce 100 mL were added.15 mL of the resulted solution was diluted to 100 mL with the same solvent. The absorbance of the solution was measured at the maximum at 263 nm, (Appendix II B.) the content of $C_{25}H_{35}NO_5$, HCl was calculated taking 263 as the value of A (1%, 1 cm) at the maximum at 263 nm. (BP, 2013)

RESULTS AND DISCUSSIONS

Formulations T1 –T6 (Change in HPMC viscosity grade)

Table 1: FormulationT1 –T6 (Change in HPMC viscosity grade).

No	Item	Apparent Viscosity (mPa.s)	T1	T2	T3	T4	T5	T6
1	Mebeverine HCL		200	200	200	200	200	200
2	HPMC E5	5.5	100	0	0	0	0	0
3	HPMC E15	14.8	0	100	0	0	0	0
4	HPMC E50	52	0	0	100	0	0	0
5	HPMC 4000	4430	0	0	0	100	0	0
6	HPMC 10 M	13929	0	0	0	0	100	0
7	HPMC K100M	79279	0	0	0	0	0	100
8	Anhydrous Lactose		20	20	20	20	20	20
9	Avecil 102		90	90	90	90	90	90
10	Aerosil	1st compression	2.5	2.5	2.5	2.5	2.5	2.5
11	Mg-Stearate		2.5	2.5	2.5	2.5	2.5	2.5
12	Aerosil*	2nd compression	1.5	1.5	1.5	1.5	1.5	1.5
13	Mg-Stearate*		1.5	1.5	1.5	1.5	1.5	1.5
15	Total wt.(mg)		418	418	418	418	418	418

Different formulations test results

Table 2: Physical and Chemical test results T1-T6.

No.	Test	T1	T2	T3	T4	T5	T6
1	Appearance	Complied	complied	complied	complied	Complied	Complied
2	Thickness	4.93	4.86	4.9	4.89	4.9	4.77
3	Diameter	11.25	11.25	11.26	11.25	11.26	11.26
4	Hardness	9.08	11.65	9.67	10.51	9.81	15.22
5	Friability	0.14	0.165	0.25	0.144	0.2	0.12
6	Average Weight	423.3	422.6	424.1	416.6	420	427
7	Assay	97.1	101.11	99.26	100.1	100.3	101.04
8	Water content	2.57	3.2	3.6	3.41	3.5	2.29

Table 3: Dissolution profiles of formulations T1 to T6.

Hrs.	T1	T2	T3	T4	T5	T6
2	61	57	32	22	19	19
3	85	90	51	30	26	29
5	90	100	69	39	36	35
7	93	102	84	45	43	40
9	95	102	92	51	49	46
11	96	102	95	56	54	51
13	97	103	96	61	58	62

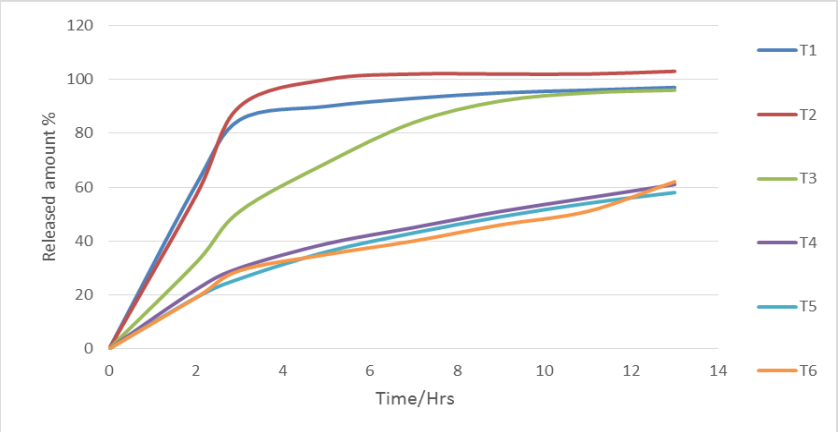

Figure 1: Dissolution profiles of formulations T1 to T6.

DISCUSSION AND CONCLUSION

In vitro release dissolution profiles of formulations (T1, T2, T3, T4, T5,and T6), with the only difference in HPMC grade (E5,E15,E50,4000,10M, and K100M) and viscosities of (5,15,50,4000,10000,and 100000mpa.s) respectively, were compressed with Round 11mm tool, Release profiles of formulations T1 (5 mpa.s), and T2 (15 mpa.s) were faster than the others with 85% and 90 % respectively in the first three hours. T3 (50 mpa.s) was more extended 92% in 9 hrs, while the release of the others (T4, T5, and T6) was very slow, less than 65% within 13 hours with close results to each other. From the results obtained it can be concluded that there is an indication of inverse relationship between the drug release and different viscosity grades, which was in agreement with the findings of (Pradhan, Budhathoki, and Thapa 2008).

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