Formulation and evaluation of vildagliptin sustained release tablets

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ABSTRACT

The main aim of proposed work was to develop Vildagliptin matrix tablets, sustained release dosage form, for the treatment anti-diabetic drug. Sustained release formulation is the drug delivery system that is designed to achieve a prolonged therapeutic effect by contineously releasing medication over an extended period of time after administration of single dose. The sustained release tablets were prepared by direct compression method using Hydroxylpropylmethyl cellulose (K15M), Dicalcium phosphate, Metalose (60SH-50) and Karayagum, Guar gum,carbopol 971P in varying ratios. Tablets blends were evaluated for loose bulk density, tapped bulk density, compressibility index and angle of repose, shows satisfactory results. The compressed tablets were then evaluated for various physical tests like diameter, thickness, uniformity of weight, hardness, friability, and drug content. Formulation F1 to F24 direct compression method, sustain release and among all the formulation, F14 formulation was compared with the marketed product for drug release pattern

Key words: Sustain release tablets, antidiabetic drugs, Hydroxylpropylmethyl cellulose

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes of administration that has been explored for systemic delivery of drugs via pharmaceutical products of different dosage form.The aim of the present study is to develop a robust formulation of anti-hyperglycemic agent as an sustained release matrix tablets. The polymers like HPMC K15M and Metalose 60 SH50 and Carbopol 971P,Guargum,karayagum, Sodium alginate were used as sustained release polymer to retard the drug release. The invitro release pattern of final formulation was compared with the innovator.Vildagliptin sustained-release formulation provides continual drug delivery over 12hours and reduces fluctuations in serum drug concentrations. This delayed release minimizes side effects related to high serum levels that occur with immediate-release formulations. It is effective, safe, and relatively well tolerated. An sustained release model drug tablet can lead to the reduction of the number of doses administered, leading to better patient compliance and less chances of overdose, in addition to which it can reduce the cost associated with treating diabetic symptoms.

MATERIALS AND METHODS

Formulations for direct compression: In this process the tablets are compressed directly from powder blends of active ingredient and suitable excipients, which will flow uniformly in to the die cavity and forms a firm compact.

Brief manufacturing procedure for the preparation of tablets: Step 1- Weighed all the ingredients separately. Step 2- The model drug and the other excipients were passed through 40# sieve together and blended for 10 minutes. Step 3- The magnesium stearate was passed through 60# sieve and added to the blend of step2 and blended for 5 minutes. Step 4- Compressed the blend of step 3 in to tablets by using 8.5mm, round punches.

Table.1.Composition of model drug formulations for direct compression

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Drug	100	100	100	100	100	100	100	100	100	100	100	100
Dicalcium Phosphate	164	149	134	119	164	149	134	119	164	149	134	119
Karayagum	30	45	60	75	0	0	0	0	0	0	0	0
Hpmck15M	0	0	0	0	30	45	60	75	0	0	0	0
Metolose60SH50	0	0	0	0	0	0	0	0	30	45	60	75
Aerosil	3	3	3	3	3	3	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3	3	3	3	3	3	3
Total(mg)	300	300	300	300	300	300	300	300	300	300	300	300

Table.2. Composition of model drug formulations for direct compression

Ingredients	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24
Drug	100	100	100	100	100	100	100	100	100	100	100	100
Dcp	164	149	134	119	164	149	134	119	164	149	134	119
Carbopol 971p	30	45	60	75	0	0	0	0	0	0	0	0
Guar gum	0	0	0	0	30	45	60	75	0	0	0	0
Sodium alginate	0	0	0	0	0	0	0	0	30	45	60	75
Aerosil	3	3	3	3	3	3	3	3	3	3	3	3
Mag.stearate	3	3	3	3	3	3	3	3	3	3	3	3
Total(mg)	300	300	300	300	300	300	300	300	300	300	300	300

RESULTS AND DISCUSSION

Table.3.Pre Compression parameters

Formulation code	Angle of Repose	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio
F1	32.59±1.06	0.59±0.36	0.68±0.31	13.46±0.44	1.18±0.37
F2	33.37±1.02	0.63±0.26	0.73±0.29	11.52±0.28	1.15±0.56
F3	29.67±0.87	0.65±0.44	0.76±0.18	14.0±0.19	1.16±0.2
F4	27.6±0.88	0.68±0.28	0.74±0.55	10.48±0.12	1.11±0.36
F5	31.16±0.95	0.63±0.52	0.73±0.25	13.17±0.34	1.16±0.26
F6	32.55±0.88	0.62±0.14	0.75±0.18	14.63±0.32	1.18±0.64
F7	33.27±0.98	0.61±0.24	0.70±0.54	10.29±0.43	1.13±0.15
F8	32.48±0.97	0.67±0.48	0.76±0.83	10.21±0.33	1.12±0.44
F9	31.6±0.65	0.64±0.17	0.69±0.25	12.05±0.54	1.16±0.27
F10	32.16±1.06	0.63±0.38	0.70±0.43	11.86±0.39	1.15±0.73
F11	33.25±0.92	0.65±0.27	0.71±0.24	13.33±0.53	1.15±0.24
F12	32.36±1.15	0.66±0.36	0.72±0.64	10.16±0.33	1.13±0.39
F13	31.28±0.68	0.63±0.32	0.66±0.34	9.27±0.21	1.12±0.17
F14	33.48±0.97	0.67±0.29	0.77±0.28	9.4±0.28	1.11±0.23
F15	30.7±0.55	0.66±0.45	0.78±0.48	9.47±0.46	1.10±0.28
F16	33.13±1.24	0.63±0.37	0.72±0.62	11.36±0.58	1.15±0.33
F17	33.26±0.62	0.67±0.49	0.76±0.29	9.47±0.23	1.10±0.19
F18	31.38±1.15	0.62±0.12	0.73±0.19	11.27±0.52	1.11±0.24
F19	30.15±0.28	0.64±0.24	0.75±0.48	13.35±0.34	1.12±0.28
F20	31.46±0.29	0.65±0.42	0.69±0.52	8.92±0.36	1.08±0.33
F21	28.4±0.15	0.68±0.58	0.78±0.75	12.38±0.27	1.10±0.42
F22	31.27±0.46	0.67±0.32	0.75±0.77	13.37±0.85	1.13±0.28
F23	30.16±0.34	0.64±0.26	0.76±0.36	9.49±0.89	1.12±0.38
F24	31.59±1.25	0.58±0.19	0.68±0.28	14.76±0.28	1.15±0.53

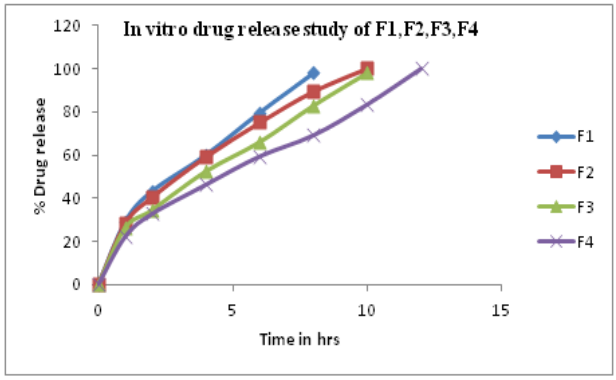

Figure.1. Cumulative % drug release of formulations F1-F4

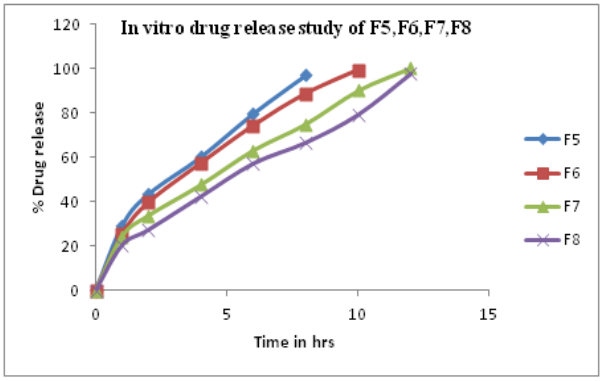

Figure.2.Cumulative % drug release of formulations F5-F8

Post Compression parameters: All the batches of tablet formulations were characterized for official evaluation parameters like Weight variation, Hardness, Friability, Tablet thickness and drug content and results are shown in the table 4.

Table.4.Characterization vildagliptin of matrix tablets

Formulation	Weight variation (mg)	Thickness (mm)	Hardness (kp)	Friability (%)	Drug content (%)
F1	300±1.08	4.44±0.4	5-7	0.18±0.03	99.24±0.49
F2	299±0.93	4.43±0.3	5-7	0.15±0.02	97.44±0.62
F3	301±0.58	4.36±0.5	5-7	0.14±0.01	98.97±1.06
F4	300±1.02	4.42±0.3	5-7	0.31±0.02	99.7±0.54
F5	300±1.37	4.43±0.5	5-7	0.13±0.01	100.18±0.54
F6	301±1.58	4.42±0.4	5-7	0.22±0.02	97.64±0.18
F7	301±0.47	4.43±0.7	5-7	0.17±0.05	98.73±0.95
F8	300±1.48	4.40±0.9	5-7	0.15±0.03	99.55±1.48
F9	300±0.97	4.38±0.8	5-7	0.19±0.08	100.33±1.22
F10	299±1.67	4.43±0.4	5-7	0.23±0.02	99.84±0.39
F11	300±0.43	4.44±0.2	5-7	0.14±0.01	99.63±1.09
F12	300±1.03	4.43±0.8	5-7	0.28±0.02	98.81±0.97
F13	301±0.75	4.48±0.6	5-7	0.27±0.04	99.59±1.08
F14	300±0.52	4.42±0.6	5-7	0.19±0.01	97.91±1.64
F15	300±0.40	4.43±0.3	5-7	0.3±0.01	100.2±1.3
F16	300±0.7	4.42±0.5	5-7	0.19±0.006	98.32±1.24
F17	300±0.23	4.43±0.8	5-7	0.18±0.016	99.18±0.57
F18	301±0.65	4.48±0.7	5-7	0.19±0.05	99.46±0.55
F19	300±0.37	4.44±0.5	5-7	0.21±0.01	99.29±1.24
F20	298±1.45	4.38±0.2	5-7	0.42±0.03	98.41±1.33
F21	299±0.43	4.43±0.4	5-7	0.22±0.01	100.34±0.74
F22	300±0.61	4.39±0.4	5-7	0.36±0.03	99.71±0.46
F23	299±0.34	4.43±0.7	5-7	0.14±0.02	99.88±1.24
F24	300±0.57	4.42±0.4	5-7	0.26±0.03	99.42±01.42

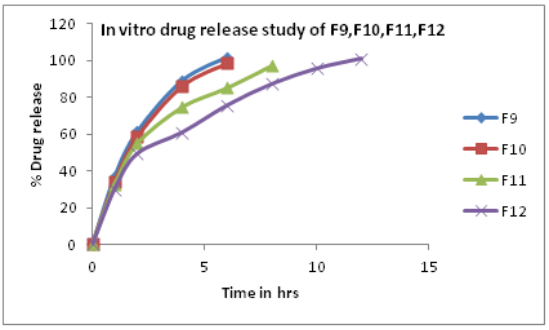

Figure.3.Cumulative % drug release of formulations F9-F12

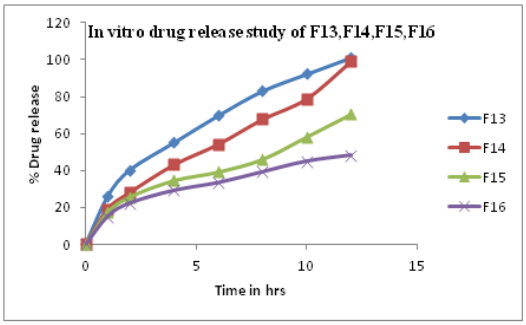

Figure.4.Cumulative % drug release of formulations F13-F16

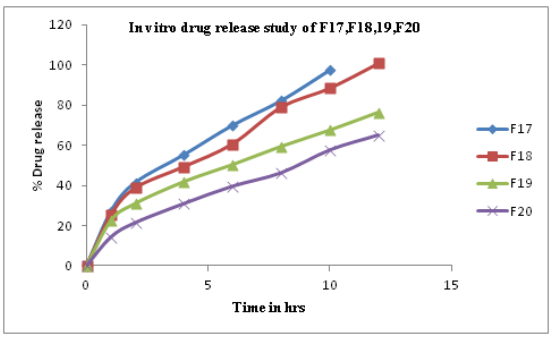

Figure.5.Cumulative % drug release of formulations F13-F16

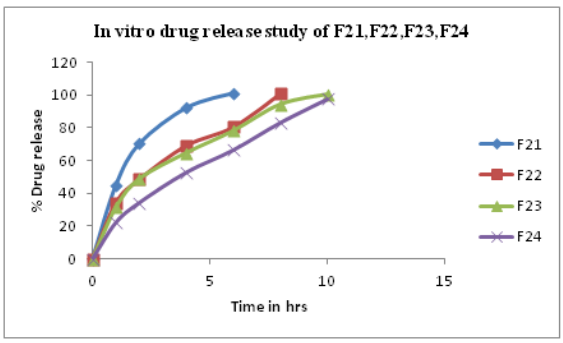

Figure.6.Cumulative % drug release of formulations F13-F16

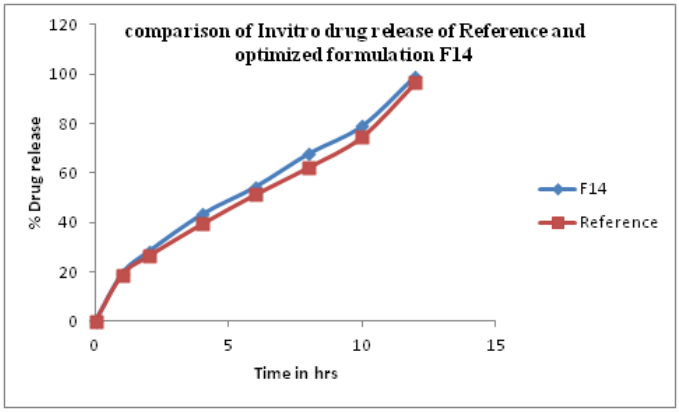

Figure.7. comparison of *In vitro* drug release of Reference and optimized F14

CONCLUSION

Sustained release tablets of a model drug were formulated and evaluated with different polymers. Formulations with Karayagum, HPMC K15M polymers has successfully sustained the model drug release upto 12 hours and they were formulated(F4&F8) in (25%concentration) 0.75:1 ratio with drug by using direct compression.Formulation prepared by using direct compression with Carbopol971P as the polymer has sustained the model drug release up to 12hours in 0.45:1 ratio NF (15% concentration) with drug. The optimized F14 formulation was compared with the marketed product for drug release pattern and was matched using similarity factor 70.11(f2) which showed that formulation F14 performed similar to the marketed product therapeutically.

REFERNCES

Basak SC, Jayakumar Reddy M, Formulation and Release Behaviour of Sustained Release Ambroxyl Hydrochloride HPMC Matrix Tablet, Int.J.Pharm, 68, 2006, 594-98.

Atul Kuksal, Ashok K.Tiwary, Narendra K, Formulation and *In vitro, In vivo* Evaluation of Extended-release Matrix Tablet of Zidovudine: Influence of Combination of Hydrophilic and Hydrophobic Matrix Formers, AAPS. Pharm.Sci.Tech, 7(1), 2006, E1-E9.

Punna Rao Ravi, Sidhura Ganga, Design and Study of Lamivudine Oral Controlled Release Tablets. AAPS PharmSciTech, 8(4), 2007, 1-9.

Shalin A. Modi, P. D. Gaikwad, V . H. Bankar, S. P. Pawar , Sustained Release Drug Delivery System : A Review, International Journal of Pharma Research and Development, 2(12), 2011,147-160.

Minakshi Marwaha, Deepak Sandhu, Rakesh Kumar M arwaha,Coprocessing Of Excipients: A Review On Exc ipient Development For Improved Tabletting Performa nce, International Journal Of Applied Pharmaceutics, 2(3),2010,41-47.

Kalam MA, Humayun M, Parvez N, Yadav S, Garg A, Amin S, Sultana Y and Ali A, Release Kinetics Of Modified Pharmaceutical Dosage Forms: A Review, Continental J. Pharmaceutical Sciences, 1(1), 2007,30-35.

Harnish Patel, Dhrupesh R. Panchal, Upendra Patel, Tushar Brahmbhatt, Mayur Suthar; Matrix Type Drug Delivery System: A Review, Journal of pharmaceutical science and biological research, 1(3), 2011, 143-151.