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Formulation and Evaluation of Duloxetine Hydrochloride (Enteric Coated) Tablets

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Duloxetine hydrochloride was tried to be formulated as enteric coated tablet using hypromellose phthalate (HP-55) as enteric coated materials in various proportions. Thus three formulations were prepared and all of them had same amount of ingredients but only difference in percentage of coating applied. *In vitro* evaluation were carried out by using U.P.S. dissolution testing apparatus. Successful formulation was found good release profile in 45 min. One commercial tablet was compared with this formulated tablets.

Key Words: Formulation, Evaluation, Duloxetine, Hydrochloride, Hypromellose phthalate.

INTRODUCTION

Duloxetine hydrochloride is a selective serotonin and norepinephrine reuptake inhibitor (SSNRI) for oral administration[1]. Generally used as treatment of major depressive disorder (MDD) and management of neuropathic pain associated with diabetic peripheral neuropathy. Orally administered duloxetine hydrochloride is well absorbed[2]. There is a median 2 h lag until absorption begins with maximal plasma concentration (Cmax) of duloxetine occurring 6 h post dose. It has an elimination half life of about 12 h (range 8 to 17 h)[3]. The most commonly adverse effect are nausea, dizziness, dry mouth, constipation, decreased appetite, fatigue, increased sweating and asthenia. The recommended dosage of duloxetine depending on the indication, preferably split into two doses per day[4].

In the present investigation, an attempt was made to formulation and evaluation of duloxetine hydrochloride enteric coated tablets. The clinical development of duloxetine showed that it is advisable to formulate in an enteric form, due to instability characteristic or degradation characteristic in acidic solution or gastic fluids. Duloxetine hydrochloride has been found to react with polymer degradation products or residual free acids present in the enteric polymers hydroxypropyl methyl cellulose acetate succinate (HPMCAS) and hydroxypropyl methyl cellulose phthalate (HPMCP) in

dosage formulations to form succinamide and phthalamide impurities respectively[1]. In this reason one separating layer was done between core tablet and enteric coating. The most suitable formulation was found in formulation[3].

EXPERIMENTAL

Duloxetine hydrochloride (Hetero Labs), primogel (DMV International), magnesium stearate (Sunshine Chemical), talcum[5] (Vijay Chemical), HPMC E-5 (Dow Chemical), poly ethylene glycol-6000 (Clariant Chemical), hypromellose phthalate (Shin Etsu Chemical) were obtained from commercial sources. All other chemical reagents were of analytical grade.

Formulation of tablets F1 to F3: All the formulations were prepared according to Table-1. Duloxetine hydrochloride, maize starch and microcrystalline cellulose load in Rmg, mix for 10 min. Prepared 10 % polyvinyl-

TABLE-1
FORMULATION OF DULOXETINE TABLETS

Ingredients (mg/unit dose)	F1	F2	F3
Duloxetine hydrochloride	33.70	33.70	33.70
Maize starch	41.30	41.30	41.30
Microcrystalline cellulose	35.00	35.00	35.00
Polyvinyl pyrrolidone	4.00	4.00	4.00
Purified water	9.5	9.5	9.5
Primogel	4.50	4.50	4.50
Mg-Stearate	0.50	0.50	0.50
Talcum	1.00	1.00	1.00
Seal coat	Wt gain 2%	Wt gain 2%	Wt gain 2%
HPMC E-5	1.20	1.20	1.20
PEG-6000	0.120	0.120	0.120
Talc	0.72	0.72	0.72
Titanium dioxide	0.36	0.36	0.36
Isopropyl alcohol	q.s	q.s	q.s
Methylene chloride	q.s	q.s	q.s
Enteric coat	Wt gain 6%	Wt gain 8%	Wt gain 10%
Hypromellose phthalate (HP-55)	5.96	7.95	9.94
Dibutyl phthalate	0.596	0.795	0.994
Talcum	0.306	0.408	0.510
Titanium dioxide	0.306	0.408	0.510
Isopropyl alcohol	q.s	q.s	q.s
Methylene chloride	q.s	q.s	q.s
Red oxide of iron	0.036	0.048	0.060

**30 mg of duloxetine equivalent to 33.70 mg of duloxetine hydrochloride.
***F1 = Formulation 1, F2 = Formulation 2, F3 = Formulation 3.

pyrolidone (PVP) solution with purified water as binding agent and slowly add to Rmg and mix for 5 min. The wet mass dried at 50 ºC in fluidized bed dryer (FBD) for 0.5 h. The dried granules load in octagonal blender primogel, Mg-stearate and talcum also load in octagonal blender and mix for 10 min. Then compress the lubricated granules using B-tooling machine. Then seal coat and enteric coat done, respectively. In formulation 1, 6 % enteric coating, formulation 2, 8 % enteric coating and formulation 3, 10 % enteric coating done.

Physical characteristic of duloxetine tablets: The dimensional specifications were measured using digital micrometer calipers. Weight variation test was conducted as per specification of IP[6]. Hardness test was preformed by using monsanto hardness tester. The friability test was preformed by using roche friabilator.

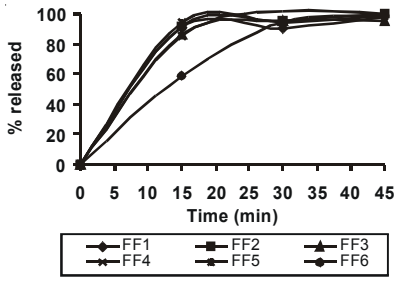
***in vitro* dissolution profile:** The dissolution profiles of duloxetine hydrochloride tablets were determined by using USP XXII apparatus-2 dissolution apparatus taking 0.1 N HCl and pH 6.8 phosphate buffer[7]. The dissolution medium of 900 mL was maintained at a temperature 37 ± 0.5 ºC. The speed of rotation of paddle was 100 rpm. The enteric coated tablet placed in the apparatus containing 0.1 (N) hydrochloric acid, withdrawn an aliquot of the fluid and proceed pH 6.8 phosphate buffer. The samples were analyzed by HPLC.

RESULTS AND DISCUSSION

The present investigation was undertaking to develop and evaluate of duloxetine hydrochloride enteric coated tablets and compare with commercial product. It was found that there was no interference to the drug with excipients. The prepared tablets and commercial tablet showed a fair uniformity of drug content of 99 to 101 %. Physical parameters were observed fairly good in the persent study conforming to requirements. Average weight of one tablet of all three formulations and one commercial tablet was found in the range 129 to 136 mg. In the present study hardness of all tablet formulations was observed in the range 68 to 80 N. Thickness of all three tablet formulations and commercial tablet were found in the range 3. 11 to 3.17 mm. Friability for all the formulations in the study was in the range of 0.028 to 0.068 %.

In vitro release profile was done in 0.1 N HCl in 2 h and then pH 6.8 phosphate buffer. The commercial tablet after 2 h of operation in 0.1 N HCl, proceed in pH 6.8 phosphate buffer media and 100 % release was shown at 45 min in buffer media. In formulation 1, two tablets out of six tablets were faild in 0.1 N HCl media using 6 % enteric coating. In formulation 2, One tablet was faild in 0.1 N HCl media using 8 % enteric coating. In formulation 3, all the six tablet were passed in 0.1 N HCl media using 10 % coating and

showed 100 % release in pH 6.8 phosphate buffer media at 45 min. Fig. 1 showed the dissolution profile of all six tablets in formulation 3. So the formulation 3 considered as a final batch which was meet all the specification of enteric coated tablets and also match with commercial duloxetine hydrochloride enteric coated tablets.



FF1 tablet 1, FF2 tablet 2, FF3 tablet FF4 tablet 4, FF5 tablet 5, FF6 tablet 6

Fig. 1. Dissolution profile of duloxetine tablets (30 mg) formulation 3

REFERENCES

1. J.J. Patrick, L.O. Peter, A.K. Craig, R.M. Steven and W.B. Steven, *J. Pharm. Sci.*, **87**, 81 (2000).
2. M.J. Detke, Y. Lu, D.L. Goldstein, R.K. McNamara and M.A. Demitrack, *J. Psychiatric Res.*, **36**, 383 (2002).
3. R.J. Lantz, T.A. Gillespie, T.J. Rash, F. Kuo, M. Skinner, H.-Y. Kuan and M.P. Knadler, *J. Drug Metabol. Disposit.*, **31**, 1142 (2003).
4. A.D. Westanmo, J. Gayken and R. Haight, *Am. J. Health Syst. Pharm.*, **62**, 2479 (2005).
5. A. Wade and P.J. Weller, Handbook of Pharmaceutical Excipients, The Pharmaceutical Press Londan, pp. 491-493 (1994).
6. Indian Pharmacopoeia, The Controller Publication, Delhi, India, p. 736 (1996).
7. SUP XXII N F XVII, United State Pharmacopoeial Convention, INC, MD, pp. 2379 and 2418 (1995).

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