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FORMULATION AND EVALUATION OF MODAFINIL FAST DISSOLVING TABLETS BY SUBLIMATION TECHNIQUE

MOTHILAL M*, A HARISH KUMAR, M CHAITANYA KRISHNA, V MANASA, V MANIMARAN, N DAMODHARAN

*Department of Pharmaceutics, SRM College of Pharmacy, SRM University, Kattankulathur -603 203, Tamilnadu.

***Corresponding author: E.mail: mothipharma78@gmail.com**

ABSTRACT

The present research work was to formulate and evaluate modafinil fast dissolving tablet by sublimation technique using camphor, menthol, thymol as sublimating agents. This method is used to sublimate the tablet which in turn increase its porosity. Modafinil is a wakefulness promoting agent for oral administration. It is only slighlt soluble in water. Therefore these tablets when kept in mouth it gets dispersed and could be easily administered to pediatric and geriatric patients. Ten formulations were planned during the study. These blends were examined in pre-compression parameters like angle of repose, bulk density, tap density, compressibility index, and Hausner's ratio. Then prepared tablets were evaluated post-compression parameters like general appearance, content uniformity, hardness, friability, mouth feel test, wetting time, disintegration, *In-vivo* dissolution studies. Tablets with camphor 7.5% show quick disintegration features. It also shows best results in wetting time, *In-vitro* dispersion test, and in-vitro dissolution studies it was shown that 104.93 % drug release within 30 minutes. Further optimized formulation was subjected to stability studies for 3 months at 25 ± 5^0c/60±5%RH&40 ± 5^0C/75±5%RH. In conclusion, the results of this work suggest that sublimation is the useful technique to enhance the solubility and dissolution rate of poorly water soluble drug like Modafinil.

KEY WORDS: Fast Dissolving tablets, Direct compression, Modafinil, Sublimating agent, Camphor.

1. INTRODUCTION

Modafinl is 2-[(R)-(diphenylmethyl) sulfinyl] acetamide ,provigil] is used in the treatment of day time sleepiness ,in narcolepsy and the other sleep disorders. It is only slightly soluble in water i.e.0.622mg/mL at 20^0c. A fast dissolving tablet can be defined as a dosage form for oral administration, which when placed in mouth, it dissolves quickly and can be swallowed in liquid. Recently fast dissolving dosage forms are popular in which they have better patient compliance due to its easiness in swallowing. Pediatric & geriatric patients may have difficulties in swallowing and chewing pharmaceutical dosage forms for oral administration. Tablets when come with contact with saliva release API by rapid disintegration/dispersion followed by dissolution of drug.

The exact mechanism of action is unknown. Modafinil belongs to a class of drugs known as Diphenylmethanes, which are stimulants that provide long-lasting mental arousal. Pharmacologically, Modafinil does not bind to or inhibit several receptors and enzymes potentially relevant for sleep/wake regulation. Modafinil is not a direct or indirect acting dopamine receptor agonist. However, in vitro, Modafinil bind to the dopamine transporter and inhibit dopamine reuptake. The precise mechanism(s) through which modafinil promotes wakefulness is unknown. Modafinil has wake-promoting actions similar to sympathomimetic agents like amphetamine and methylphenidate, although the pharmacologic profile is not identical to that of sympathomimetic amines.

Modafinil has weak to negligible interactions with receptors for norepinephrine, serotonin, dopamine, GABA, adenosine, histamine-3, melatonin, and benzodiazepines. Modafinil also does not inhibit the activities of MAO-B or phosphodiesterases II-V. FDT are the dosage form with disintegrating rate in patients mouth within a few seconds without need of water (or) chewing, providing to the patients who are suffering from dysphasia. The advantage of mouth dissolving dosage form is increasing now a days in industrial areas. The basic approach used in the development of the mouth dissolving tablets is to formulate modafinil by sublimation method. The independent variables were selected as the quantities of Cross povidone, as super disintegrating agents, Aspartame as sweetener, (Camphor, Menthol, thymol) as sublimating agents,mannitol as diluent However , MCC diclacium phosphate & L-HPC were excluding in formulation as they cause an unpalatable feeling of grittiness in mouth. Modafinil is 2-[(R)-(diphenylmethyl) sulfinyl] acetamide. It is widely used as wakefulness promoting agent for oral administration. It is a recemic compound each tablet contains 100 mg of Modafinil. The emperical formula is $C_{15}H_{15}NO_2S$ & the molecular weight is 273.35. This is Very slightly soluble or practically insoluble in water, sparingly soluble in methanol, slightly soluble in ethanol. The Melting Point is 160-165 ºC. It is a white to off-white, crystalline powder According to Bio Pharmaceutical classified system (BCS) it belongs to a class of drugs known as Diphenylmethanes, which are stimulants that provide long-lasting mental arousal. In present study, an attempt was made to develop mouth

dissolving tablets of Modafinil and to find the effect of wetting time, disintegration time, *in-vitro* dispersion test and *in- vitro* dissolution test in tablets.

2. MATERIALS AND METHODS

Modafinil is the gift sample from Suryan pharmaceuticals (Chennai, India),Camphor from Indian research products (Madras, India), Thymol from Sisco research laboratories Private limited (Mumbai, India), Menthol from (Indian research products (Madras, India) peppermint from Indian research products (Madras, India) Cross povidone from Fourtees (Chennai, India), Aspartame from Fourtees (Chennai, India) Aerosol from Sisco research laboratories Private limited (mumbai ,india),Magnesium stearate from LOBA CHEMIE Private Limited (Mumbai, India), Mannitol from Rankem (New Delhi, India).

Characterization of drug and excipients

Fourier Transform Infra Red Spectroscopy (FTIR): FTIR spectra of pure Modafinil and physical mixture of drug and excipients were recorded on Shimadzu Corporation, (Tokyo, Japan) Model-1601 PC. Potassium bromide pellet method was employed and background spectrum was collected under identical situation. Each spectrum was derived from single average scans collected in the region 400- 4000 cm^{-1} at spectral resolution of $2cm^{-2}$ and ratio against background interferogram. Spectra were analyzed by software supplied by Shimadzu.

Formulation method: Fast dissolving tablets of Modafinil were prepared by direct compression method according to the formula given in Table 6. Modafinil, menthol, camphor, thymol at variable proportions which reused as sblimating agents and Superdisintegrants (CPXL10) were thoroughly mixed for about 10 min. Then add aspartame, aerosol, mannitol, peppermint, and to above mixer and lubricated with Magnesium Stearate. The lubricated blend then compressed in to oval shape tablets 10mm punch (Cadmach automatic Punching Machine) to get a tablet of 200 mg of weight. After punching keep the tablets of formulations MMS1-MMS9 in hot air oven at 60^0c for 60 min. Where as in MMS10 it is not heated in hot air oven and hence evaluated directly.

Tab 1: Formulation and evaluation of Modafinil mouth dissolving tablets by sublimation technique

Ingredients (mg)	MFS1	MFS2	MFS3	MFS4	MFS5	MFS6	MFS7	MFS8	MFS9	MFS10
Modafinil	100	100	100	100	100	100	100	100	100	100
Camphor	10	15	20	-	-	-	-	-	-	-
Menthol	-	-	-	10	15	20	-	-	-	-
Thymol	-	-	-	-	-	-	10	15	20	-
Cross povidone	4	4	4	4	4	4	4	4	4	4
Aspartame	2	2	2	2	2	2	2	2	2	2
Peppermint	2	2	2	2	2	2	2	2	2	2
Aerosil	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2	2
Mannitol	78	73	68	78	73	68	78	73	68	88
Total weight(mg)	200	200	200	200	200	200	200	200	200	200

Scanning of λ max: The calibration curve was based on the spectrophotometry; 100mg of drug was taken dissolved in ethanol and make up the volume to 100 ml with 0.1N HCL. From the above solution 10ml was taken made up to 100 m with0.1N HCL. 10 ml was taken and made up to 100ml with ethanol (10µg/ml) and this solution was scanned between 200 – 400nmin UV spectrophotometer. The maximum absorption was observed at 222nm. It obeys Beer's law in the concentration range of 4-24 µg/mL.

Preparation of Standard Curve: Standard stock solution : The stock solution was freshly prepared by dissolving 100 mg of Modafinil in few ml of Ethanol (5ml) in a 100 ml volumetric flask and then made up the solution up to the mark using 0.1NHCL for obtaining the strength of 1000µg/ml (stock I). 10 ml of this solution was diluted to 100ml with 0.1NHCL to obtain a solution of strength 10µg/ml (stock II). From the secondary stock 0.4, 0.8, 1.2, 1.6, 2.0, and 2.4 ml, was taken separately and made up to 10ml with 0.1NHCL to Produce 4, 8, 12 ,16, 20 and 24 µg/ml respectively. The absorbance was measured at 222nm using a UV spectrophotometer.

Pre-Compression Characters: Formulated granule blends were analyzed for its Angle of repose, Bulk density, Tap density, from this Hausner's ratio and Compressibility index were obtained.

Post-Compression Characters:

Physical Appearance: The physical appearance of the compressed tablets involves the measurement of a number of attributes like tablet shape, smoothness, chipping, cracks, surface texture, color, embossing, de-bossing.

Thickness: Thickness was determined for 20 pre weighed tablets of each batch using a digital vernier scale and the average thickness was determined in mm. The tablets thickness should be controlled within a +/- 5% variation of standard.

Weight variation: 20 tablets were selected randomly from a batch and were weighed individually and then average weight was calculated. The tablets meet the USP specifications if not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Hardness test: The crushing load which is the force required to break the tablet in the radial direction was measured using schluenzier hardness tester. The hardness of 10 tablets was noted and the average hardness was calculated. It is given in KP.

Percentage friability: In friability testing the tablets are subjected to abrasion and shock. It gives an indication of the tablets ability to resist chipping and abrasion during transportation and shipping. The % friability is expressed as the loss of weight and is calculated by formula $\%friability = (w_o - w_f) / w_o \times 100$

W_o – initial weight of tablets

W_f – final weight of tablets

Wetting time: A piece of tissue paper folded twice with (ID=6.5 cm) cutted and 6.8 ml of pH buffer was placed and the tablet was kept ,time taken to swell and crack obtaining on the surface of the tablet was measured and 3 trials were made for all the formulations.

***In vitro* Dispersion test:** *In-vitro* dispersion test is done by taking 10 ml of pH 6.8 buffer in measuring cylinder. Then place tablet into it and watch under stop clock how much of seconds needed to disperse the tablet in medium.

Disintegration time: It is the time taken by the tablet to breakup into smaller particles. The disintegration test is carried out in an apparatus containing a basket rack assembly with six glass tubes of 7.75cm in length and 2.15mm in diameter, the bottom of which consists of a 10 mesh sieve. The basket is raised and lowered 28 – 32 times per minute in a medium of 900ml which is maintained at 37 ± 2^0 c. Six tablets were placed in each of the tubes and the time required per complete passage of tablets garments through the 10 mesh was considered as the disintegration time of the tablet.

Dissolution Studies: Medium: 0.1 N Hydrochloric acid, 900 ml, Apparatus II, 50 rpm, time: 60 minutes.

Stability Studies: Stability studies were carried out on optimized formulation as per ICH specifications. The tablets were stored at 25 ± 2^oC / 60 ± 5% RH and 40 ± 2^oC / 75 ± 5% RH for duration of three month. After an interval of one month samples were withdrawn and tested for various physical tests and *in-vitro* drug release.

3. RESULTS

Pre-compression parameters: The standardization of Modafinil was done at 222nm and its equation was given as y = 0.031x + 0.229 and its R^2 was given as 0.992 Compatibility study was done for the powder mixture of drug with Crosspovidone and sublimating agents. It was found that the drug is compatible with the excipients. Water insoluble diluents such as micro crystalline cellulose, Dicalcium phosphate were excluded in the formulation as they may cause an unpalatable feeling of grittiness in the mouth. Among the soluble diluents Mannitol was identified for its advantages of smooth feeling negative heat of dissolution with the results of some preliminary experiments for selecting super disintegrants, Crosspovidone was identified which showed to fastest disintegration. Aspartame was used as sweetener at a blend of 1%w/w to mask the bitter taste of Modafinil. Sublimating agents such as camphor, menthol, and thymol were used to increase porosity of the tablets.

Modafinil fast dissolving tablets were prepared by direct compression method using sublimation technique. The formulated tablets were evaluated for post formulation parameters like weight variation, hardness, Friability, Thickness, Disintegration time, wetting time, Drug content, *In-vivo* dispersion test. The weight of single tablet was targeted as 200 mg and hence the % deviation accepted as per USP is 7.5 %. 20 tablets were selected randomly from all batches and weighed individually. Average weight was calculated. The weight variation values for all the batches were found to be within the acceptable limits. The percentage friability for the formulated batch MMS1to MMS10 was found to be within 0.2-0.6 range. The acceptable limit as per USP is 1%. Disintegration time for Modafinil mouth dissolving tablets is 3 mins as per U.S.P.

All the formulations were found to be within the limits. Formulations MMS1-MMS10was found to be 18-180 sec Best formulation was found to be MMS2 within 18 seconds. Over all best formulations was found to be MMS2. For the entire formulated batch from MMS1-MMS10 the drug content was found to be 98.87-100.16.*I*n release studies

was carried out using USP type 2 paddle apparatus at 37± 0.5^{0}c taking 900 ml of pH 1.2 dissolution medium speed of rotation was set to 50 rpm. Aliquots of 5 ml was withdrawn at 5, 10, 20, 30, 45, 60 min and analyzed spectrophotometrically at 222nm. The *I*nvitro profile shown in the figure: indicated faster and maximum drug release from formulation MMS2. The MMS2 by direct compression in sublimation technique of camphor shown release of 104.98% of drug at the end of 30 min .where as in marketed formulations shown in fig: 3, the marked formulation *I*n vitro drug release was done. Aliquots were withdrawn at 15, 30, 45, 60, 90,120 min and at the end of 120 min it shows 99.94% drug release.

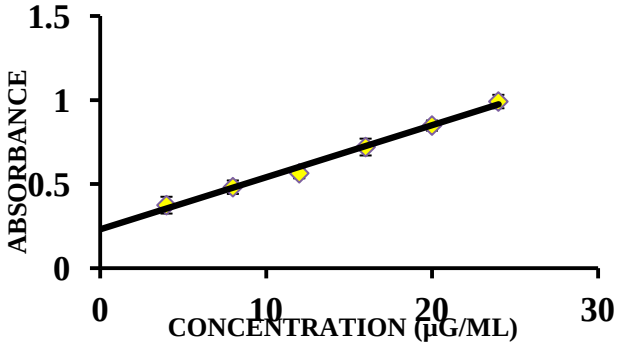

Figure: 1 Standard curve of Modafinil in 0.1 N Hcl at 222 nm

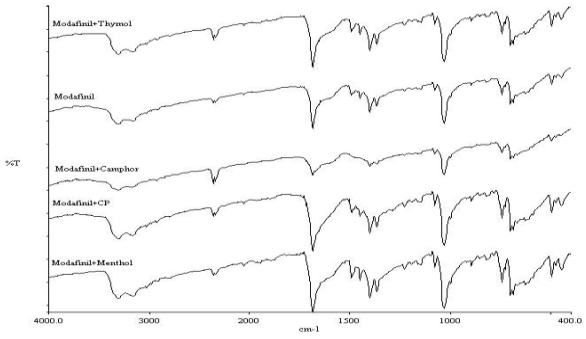

Figure 2: IR Spectra of Modafinil and its combination with CP, Camphor, Menthol, Thymol

Tab 2: Pre-formulation character of Modafinil Mouth Dissolving Tablet

Formulation Code	Angle of Repose	Bulk Density (g/ml)	Tapped Density (g/ml)	Hausner's Ratio	Compressibility Index
MMS_1	25.31±0.02	0.5±0.02	0.6±0.02	1.20±0.05	16.67±0.04
MMS_2	26.82±0.01	0.62±0.01	0.72±0.01	1.16±0.01	13.89±0.01
MMS_3	27.61±0.03	0.54±0.04	0.65±0.03	1.20±0.02	16.92±0.02
MMS_4	26.57±0.04	0.58±0.03	0.68±0.04	1.17±0.03	14.71±0.03
MMS_5	25.67±0.02	0.67±0.03	0.9±0.02	1.34±0.04	25.56±0.02
MMS_6	25.94±0.01	0.54±0.02	0.64±0.02	1.19±0.01	15.63±0.01
MMS_7	27.58±0.02	0.67±0.02	0.78±0.01	1.16±0.01	14.10±0.04
MMS_8	26.34±0.04	0.68±0.03	0.82±0.03	1.21±0.02	17.07±0.03
MMS_9	28.23±0.02	0.59±0.04	0.75±0.02	1.27±0.03	21.33±0.02
MMS_{10}	25.72±0.02	0.61±0.04	0.76±0.03	1.25±0.04	19.74±0.04

Tab 3: Evaluation of Post compression studies

Formulation Code	Hardness (kg/cm$^{2)}$	Friability (%)	Thickness (mm)	Weight Variation (mg)
MMS_1	3.2±0.02	0.2±0.02	4.14±0.02	199.7±0.03
MMS_2	3.3±0.01	0.25±0.01	4.11±0.01	200.2±0.01
MMS_3	3.2±0.02	0.3±0.03	4.12±0.02	208.2±0.02
MMS_4	3.2±0.04	0.4±0.04	4.61±0.03	199.7±0.03
MMS_5	3.2±0.05	0.5±0.02	4.69±0.02	205.6±0.02
MMS_6	3.4±0.06	0.6±0.03	4.67±0.02	202.9±0.01
MMS_7	3.5±0.02	0.3±0.04	4.62±0.01	199.5±0.02
MMS_8	3.5±0.01	0.2±0.03	4.96±0.02	202.5±0.03
MMS_9	3.4±0.02	0.2±0.05	4.99±0.02	203.4±0.02
MMS_{10}	3.2±0.04	0.3±0.02	4.5±0.03	205.1±0.03

Tab 4: Evaluation of Post compression studies

Formulation code	Disintegration time (s)	*In-vivo* dispersion test (s)	Wetting time (s)	Drug content (%)
MMS_1	19	25	25	100
MMS_2	18	22	21	100
MMS_3	25	28	22	100.16
MMS_4	22	29	27	99.19
MMS_5	29	23	25	99.35
MMS_6	25	28	29	98.87
MMS_7	26	27	22	99.35
MMS_8	26	26	28	99.67
MMS_9	24	24	26	100
MMS_{10}	180	140	230	100

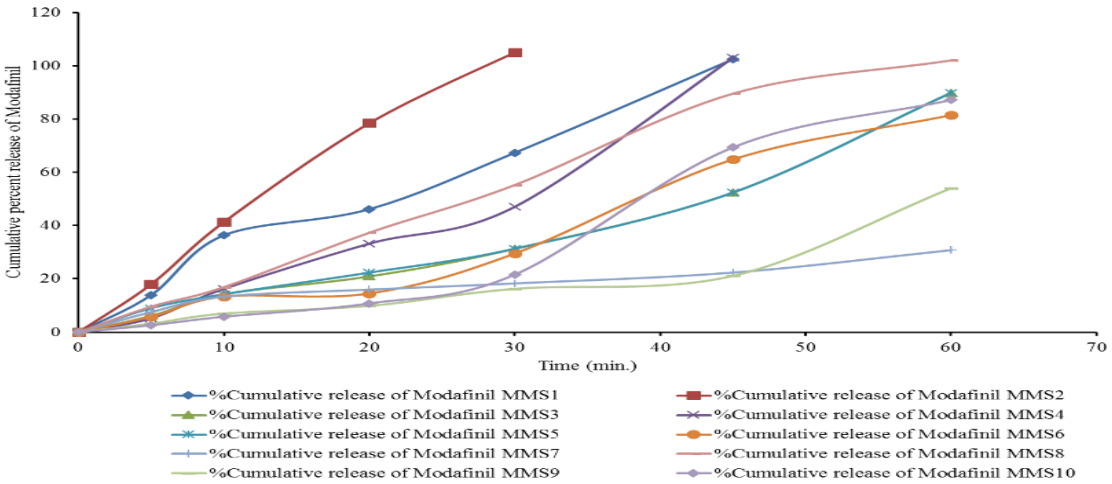

Fig 3: % Cummalative release of modafinil MMS1-MMS10

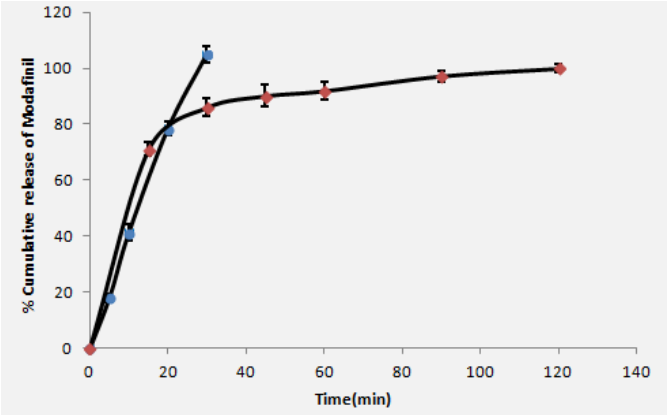

Fig 4: Comparative study of marked formulation and optimized formulation MMS_2

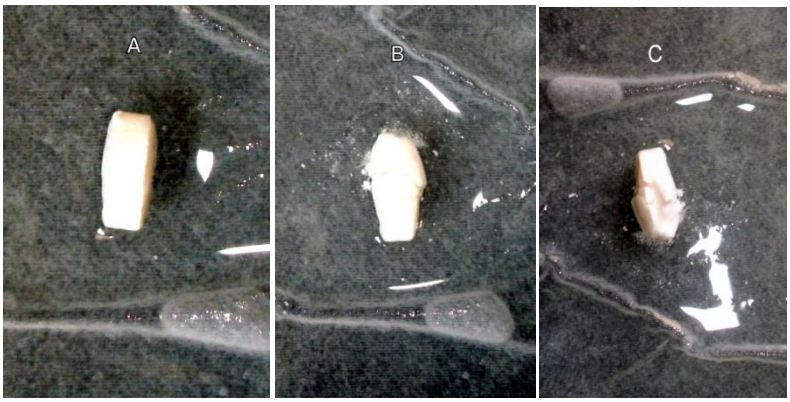

Fig: 5 Different stages of tablet in wetting time

CONCLUSION AND SUMMARY

The aim of the present research work was to develop fast dissolving tablets of Modafinil by sublimation technique. Ten formulations using cross povidone as super disintegrant and camphor, menthol, thymol as sublimating agents were prepared. These formulations were evaluated for pre-compression parameters and post-compression parameters. Pre-compression parameters such as tapped density, bulk density, angle of repose hausner`s ratio, compressibility index were performed. Post compression parameters such as disintegration test, *In-vitro* dispersion test, wetting time and *In-vitro* dissolution test, friability test, weight variation test were performed. Based on the above evaluations, Formulation code FMS_2, which shown less disintegration time of 18 sec and 104.98% of drug released within 30 min while the marketed formulation took 2 h.

REFERENCES

Aulton ME, Pharmaceutics, Tablets and compaction, In the Science of Dosage Form Design, 2, 2007, 404-408.

Azeem S, Immediate Release Drug Delivery Systems, A Review, Int journal of biopharma and toxi R, 1(1), 2011, 24-46.

Bentley's, Rawlins EA, Textbook of Pharmaceutics, Eighth Ed, 2003, 270-281.

Biederman J, Swanson JM, Wigal SB, Kratochvil CJ, Boellner S W, Earl C Q, Jiang J, and Greenhill L, Efficacy and Safety of Modafinil Film-Coated Tablets in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder: Results of a Randomized, Double-Blind, Placebo-Controlled, Flexible-Dose Study Pediatrics, American Academy of Pediatrics, 116, 2005, 777 – 784

Chandria R.M, Jaykar B, Chakrabarty B.L, Formulation and evaluation of Orodispersible tablets of Terbutaline sulphate, Drug Invention Today, 2(1), 2010, 31-33

Chien, YW, Oral Drug Delivery Systems, In Novel Drug Delivery Systems, 1990, 139-141

Debjit B, Chiranjib B, Krishnakanth P, Fast Dissolving Tablet: An Overview, J. Chem & Pharm R, 1(1), 2009, 163-177

Gabrielsson J, Lindberg N and Lundstedt T, Multivariate methods in pharmaceutical applications, J.Chemom, 16, 2002, 141-160

Gudas G. K, Manasa B., Rajesham V.V, Kumar S.K, Kumari J.P, Formulation and evaluation of fast dissolving tablets of Chlorpromazine HCl J, Pharmaceutical Sci & Tech., Vol.2(1), 2010, 99-102

Gupta A, Mishra A.K, Gupta V, Bansal P, Singh R, Singh A.K, Recent Trends of Fast Dissolving Tablet - An Overview of Formulation Technology, Int J. of Pharma& Bio Archs., 1(1), 2010, 1-10

Kumar P, Pasupathi A, Chandira M, Bhowmik D, Chiranjib, Jayakar B, Formulation and evaluation of fast dissolving tablets of Rupatadine fumarate Der Pharmacia Lettre, 1 (2), 2009, 151-163

Lachmann H.A, and Libermann L, Kanik, Theory and practice of industrial pharmacy, 2000, 293-329.

Li J, and Mei X, Applications of Cellulose and Cellulose Derivatives in Immediate Release Solid Dosage ACS Symposium Series, Vol. 934Polysaccharides for Drug Delivery and Pharmaceutical Applications Chapter 2, 19-55.

Libermann H.A, Lachmann L, Schwartz, B.J, Pharmaceutical dosage forms, Tablet vol I, second ed. revised and expanded, 2000, 106-160.

Mahamuni S B, Shahi S R, Shinde N V, Agrawal G.R, Formulation and Evaluation of Fast Dissolving Tabets of Promethazine Hc with Taste Masked Bitter Taste Int J, Pharma R & Development Online, 2009 (7) 1-18

Mahapatra A.K, Murthy P.N, Pradhan S.P, Solubilization and Solid-State Characterization of Modafinil Solid Dispersions using PVP K 30 Der Pharmacia Lettre, 3(1), 2011, 29-37

Natarajan R, Vaishnani R, Rajendran, NN, Formulation and Evaluation of Immediate Release Tablets of Paroxetine HCl Using Different Superdisintegrants Int. J, Re Pharm and Biomedical Sci., Vol. 2 (3), 2011, 1095-1099

Parikh B.N, Patel D.M, Patel C.N, Dave J.B, Gothi G.D, Patel T.D, Formulation Optimization and Evaluation of Immediate Release Tablet of Telmisartan, J. Global Pharma Tech., 2(2), 2010, 79-84.

Pathak N, Kumar Anuj, Methkar Vishal, Pant P, Rao R.T, Formulation and Optimization Immediate Release of an Antialcohoic Drug by Dry Granulation Method., Pharmacie Globale (IJCP), 2(3), 2011, 1-4

ReddyV.P, PriyaV.A.V, Rao G.C.S, Reddy D.S, The effect of different superdisintegrants and their concentrations on the dissolution of topiramate immediate release tablets, Int J Pharma Sci and Nano techn, 2(2) ,2009, 531- 536

Rowe, R. C, Handbook of Pharmaceutical Excipients 5th edition, 2006, 132-135, 211-213, 214-216, 611-616, 701-704

Sahoo S, Mishra B, Biswal P.I. K, Panda O, Mahapatra S.K, Jana G. K, Fast Disslving Tablet: As a potential drug delivery system, drug invention today, 2, 2010, 130-133

Setty C.M., Prasad D.V.K., Gupta V.R.M., Development of fast dispersible aceclofenac tablets: Effect of functionality of superdisintegrants, Indian J Pharm Sci,70, 2008, 180-185

Shirsand S.B, Suresh S, Swamy P.V, Para M.S, Kumar D.N, 2010, Formulation design of fast disintegrating tablets using disintegrant blends. Indian J Pharm Sci, 72:130-3

Shirsand S.B, Suresh S, Swamy P.V, Para M.S., Kumar D.N., 2010, Formulation design of fast disintegrating tablets using disintegrant blends. Indian J Pharm Sci, 72:130-3

Singh S K, Mishra D N, Jassal R, Soni P, Fast Disintegrating Combination Tablets Of Omeprazole and Domperidone Asian Journal of Pharmaceutical and Clinical Research, 2 (3), 2009, 75-82

Swathi, Neeharika V and Lakshmi PK, Formulation and evaluation of fast dissolving tablets of freely and poorly soluble drug with natural and synthetic super disintegrants , Drug invention today, 3(10), 2011, 250-256 .

U.S.P. (United States Pharmacopiea) 2011, vol- III, 3548

Vasanthkumar S, Vijaya RC, Immediate release tablets of telmisartan using superdisintegrant-formulation, evaluation and stability studies, Chem. Pharm. Bull, 56(4), 2008, 575—577

Vineet Bhardwaj, Mayanak Bansal and Sharma P K, formulation and evaluation of oral fast dissolving tablets of Camphor as using sublimating agent, Am-Euras. J. Sci. Res, 5(4), 2010, 264-269.

Watanable Y, Preparation of rapidly disintegrating tablets using new type of MCC (PH-M-Series) and L-HPC by direct compression method, Chemical Pharm Bull, 49(2), 2001, 134-139

Yeole CN, Darekar SS, Gupta A, Shrinivasan G, Formulation and evaluation of immediate release tablets of paroxetine HCl, J Pharma R, 3(8), 2010, 1736-1738.

Zhao N, Augsburger LL, the influence of swelling capacity of superdisintegrants in different ph media on the dissolution of hydrochlorthiazide from directly compresed tablets, AAPS, Pharmsci, 06(1), 2005, 42.