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Fabrication and assessment of Levofloxacin controlled release tablets

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ABSTRACT

Vividly Oral drug delivery method is the most widely utilized routes for administration among all alternatives that have been explored for systemic delivery of drug via various pharmaceutical products of different dosage forms. Popularity of the route may be ease of administration as well as traditional belief that by oral administration the drug is due to the well absorbed into the food stuff ingested daily. The present work is aimed at preparing and evaluating Controlled-release (CR) matrix tablets of Levofloxacin using different polymers. From the results, formulationf6 containing Levofloxacin 250 mg, Xanthum gum evolved as the optimized formulation. The result revealing shows the feasibility of fabricating levofloxacin controlled release tablets significantly with better drug release profile.

Keywords: Controlled release tablets, Levofloxacin, Fabrication & drug release

INTRODUCTION

Sustained release (S.R)/ Controlled release (C.R) pharmaceutical products have gradually gained medical acceptance and popularity. Regulatory approval for marketing and their pharmaceutics superiority and clinical benefits over immediate release pharmaceutical products have been increasingly recognized. Modified release oral dosage forms have brought new lease of life into drugs that have lost market potential due to requirement of frequent dosing, dose related toxic effects and gastrointestinal disturbances [1-8].

The term modified-release drug products used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms as presently recognized [9-15].

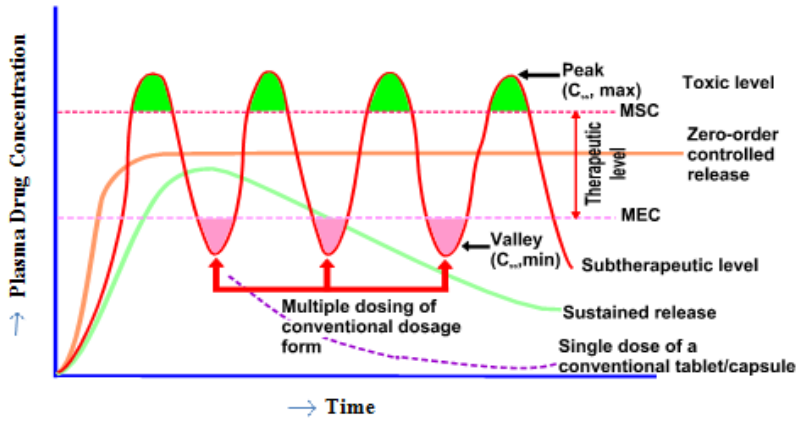


Figure 1: A hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of sustained and controlled delivery formulations.

Rationale of Controlled Drug Delivery

The basic rationale for controlled drug delivery is to alter the pharmacokinetic and pharmacodynamics of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and/or physiological parameters inherent in a selected route of administration. It is desirable that the duration of drug action become more to design properly. Rate controlled dosage form, and less, or not at all, a property of the drug molecules inherent kinetic properties. As mentioned earlier, primary objectives of controlled drug delivery are to ensure safety and to improve efficiency of drugs as well as patient compliance [16-19].

MATERIALS AND METHODS

Levofloxacin has been obtained as a gift sample from Aurobindopharma, all other recipients are obtained from the reputed manufactures

LEVOFLOXACIN

Description

Nomenclature

Chemical Name

(*S*)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-7*H*-pyrido[*1,2,3-de*]-1,4-benzoxazine-6-carboxylicacid

Formula

Empirical formula: $c_{18}h_{20}fn_3o_4$

Structural Formula

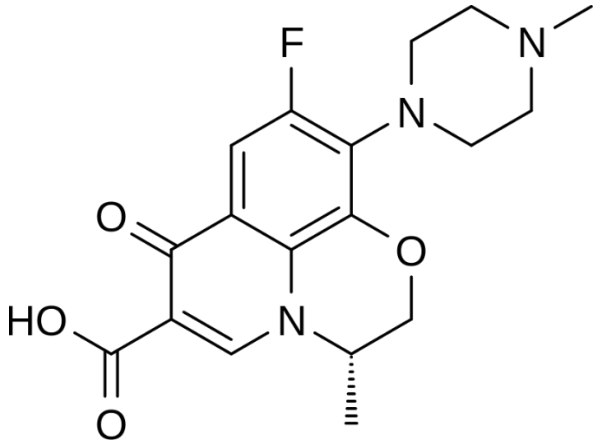


Figure 2: Structure of Levofloxacin

Physical and Chemical Properties

- **Molecular weight -** 361.4
- **Color-** White
- **Nature-** Crystalline powder
- **Odour -** Odourless

Mechanism of Action

Levofloxacin inhibits bacterial type II topoisomerases, topoisomerase IV and DNA gyrase. Levofloxacin, like other fluoroquinolones, inhibits the A subunits of DNA gyrase, two subunits encoded by the **gyra**gene. This results in strand breakage on a bacterial chromosome, supercoiling, and resealing; DNA replication and transcription is inhibited.

Half Life: 6-8hr

Bio-Availability: 99%

Construction of Standard Graph of Levofloxacin

Accurately weighed amount of 100 mg of Levofloxacin was transferred into a100 ml volumetric flask. Methanol was added to dissolve the drug and the primary stock solution was made by adding 100 ml of methanol. This gives a solution having concentration of 1mg/ml of Levofloxacin stock solution. The absorbance was measured at 245 nm using a UV spectrophotometer (Systronic, Hyderabad, India).

Preparation of Levofloxacin Matrix Tablets

All the matrix tablets, each containing 250 mg of Levofloxacin, were prepared by direct compression method and also to study the effect of various ratios of different types of polymers on the drug release.

Direct compression method

Accurately weighed quantity of labetolol taken into the motor pestle and slowly add the polymer mixture & filler with spatula (Tumbling method) then stir well Scrap until it reaches to Room temperature Pass through 22 No. Mesh and the through 44 no sieve to separate the granules and fines. Finally add talc and magnesium stearate to the granules.

Formulations

In formulations prepared, the release retardants included were Xanthum gum, Hydroxypropylmethylcellulose (HPMCK4M). Microcrystalline cellulose (MCC) was used as diluents. Magnesium stearate (MS) 1% and talc 2 % were used as lubricants. Compositions of different formulations were given in the following Table.

Table 1 .Composition of Matrix Tablets Containing Carbopol934P

Ingredients(mg/tab)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Levofloxacin	250	250	250	250	250	250	250	250	250
HPMC K100	150	200	250	-	-	-	-	-	-
Guargum	-	-	-	150	200	250	-	-	-
Xanthumgum	-	-	-	-	-	-	150	200	250
MCC	245	195	145	245	195	145	245	195	145
Magnesium stearate	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3

Evaluation of Precompression Blend

- Angle of Repose
- Determination of Bulk Density and Tapped Density
- Compressibility Index (Carr's Index)
- Hausner's Ratio

Evaluation of Matrix Tablets

- Thickness
- Hardness
- Friability Test
- Weight Variation Test

Drug Content (Assay)

Three tablets were weighed and taken into a mortar and crushed into fine powder. An accurately weighed portion of the powder equivalent to average weight of three tablets of Levofloxacin was transferred to a 100 ml volumetric flask containing 6.8 ph Phosphate buffer solution and the volume was made upto the mark. From this 10ml was taken and shaken by mechanical means using centrifuge at 3000rpm for 30min. Then it was filtered through whatman filter paper. From this resulted solution 1 ml was taken, diluted to 10 ml with 6.8 ph Phosphate buffer solution and absorbance was measured against blank at 245 nm. [13-16]

In -vitro Drug Release Characteristics

Drug release was assessed by dissolution test under the following conditions: n = 3, USP type II dissolution apparatus (paddle method) at 50 rpm in 900 ml of and the phosphate buffer ph 6.8 upto 24 hours and temperature was maintained at 37°C ± 0.5°C. An aliquot (5ml) was withdrawn at specific time intervals and replaced with the same volume of prewarmed (37°C ± 0.5°C) fresh dissolution medium. And drug content in each sample was analyzed by UV-visible spectrophotometer at 245 nm. [20, 21]

Fourier Transform Infrared Spectroscopy (FTIR) Studies

FTIR studies were performed on drug and the optimized formulation using Shimadzu FTIR (Shimadzu Corp., India). The samples were analyzed between wavenumbers 4000 and 400 cm^{-1}.

RESULTS AND DISCUSSION

Characterization of active pharmaceutical ingredient

In pre formulation studies, characterization of API (appearance, identification test by FTIR, assay) was performed and it was found that all are within the range specified in the pharmacopoeia.

Calibration Curve of Levofloxacin in 6.8ph

Standard graph of Levofloxacin was constructed using 6.8 ph phosphate buffer. Various concentrations 2 to 10 µg/ml were prepared. The absorbance of prepared concentrations was measured at 245(6.8 ph) nm by adjusting to zero with blank sample.

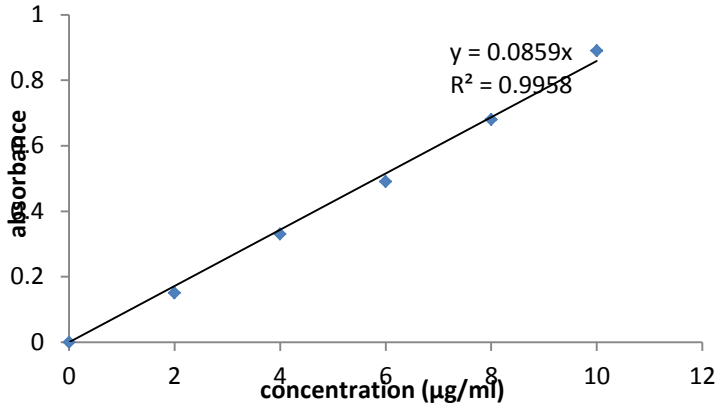


Figure 3: Calibration curve in 0.1N hcl

Precompressional parameters

Before preparation of floating tablets of Levofloxacin, the powder mass is evaluated for flow properties. The results of flow properties are shown in below Tables. All the prepared formulations showed good flow properties.

Table 2: Pre compression parameters

Formulation Code	Bulk Density	Tapped Density	Carr's Index	Hausner Ratio	Angle of Repose
F1	0.55	0.65	1.25	0.25	23.45
F2	0.54	0.62	1.19	0.16	19.65
F3	0.56	0.64	1.23	0.18	22.35
F4	0.54	0.63	1.12	0.11	20.69
F5	0.50	0.67	1.24	0.22	20.82
F6	0.53	0.64	1.23	0.18	20.72
F7	0.51	0.67	1.24	0.19	20.89
F8	0.52	0.69	1.3	0.23	20.78
F9	0.56	0.68	1.21	0.17	22.6

Post compression parameters

The results of the weight variation, hardness, thickness, friability, and drug content of the Tablets are given in table

Table 3: Post compression parameters

Formulation Code	Thickness (mm)	Weight Variation(mg)	Friability (%)	Hardness	%Drug Content
F1	3.41	649.6	0.16	5.4	96.19
F2	3.45	648.75	0.18	5.5	99.69
F3	3.43	650.67	0.17	5.3	99.77
F4	3.35	649.40	0.25	5.6	100.38
F5	3.54	650.56	0.22	5.3	99.38
F6	3.60	649.67	0.3	6.0	96.5
F7	3.63	649.40	0.48	5.6	99.49
F8	3.72	650.89	0.25	5.5	98.17
F9	3.46	650.7	0.42	5.0	99.38

Swelling Index

Table 4: Swelling index data

Formulation Code	Swelling Index±SD
F1	22.4
F2	24.07
F3	23.67
F4	28.63
F5	29.76
F6	31.80
F7	38.69
F8	29.45
F9	30.12

Dissolution Profiles of Formulations

Table 5: *In vitro* release profile

Time (hr)	Percentage drug release(%)								
	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	9.7	10.5	10.5	18.5	15.5	15.6	9.6	21.2	15.6
4	15.6	15.8	15.6	24.6	21.6	28.5	15.7	35.4	24.5
6	25.5	26.9	28.5	35.6	30.5	36.7	22.9	46.7	28.9
8	38.9	49.8	39.6	41.7	39.5	58.5	35.6	58.9	45.6
10	65.8	70.2	54.6	60.7	51.8	78.28	43.2	67.9	58.9
12	79.8	85.4	68.9	78.9	70.9	97.8	55.2	81.5	69.8

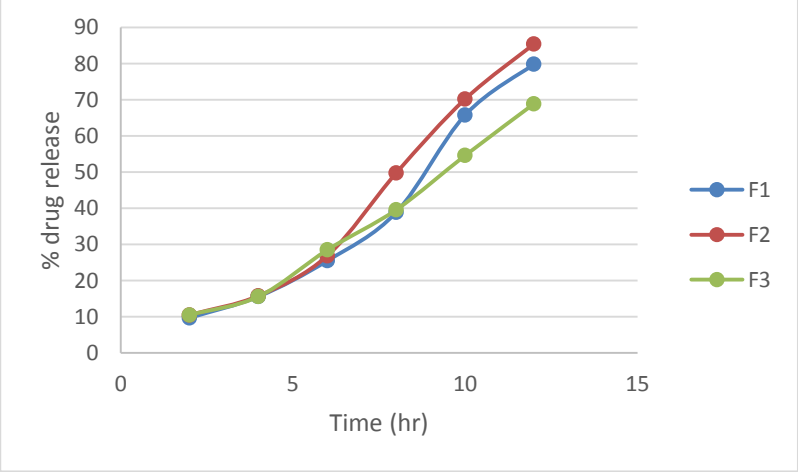


Figure 4: Percentage drug release (F1-F3)

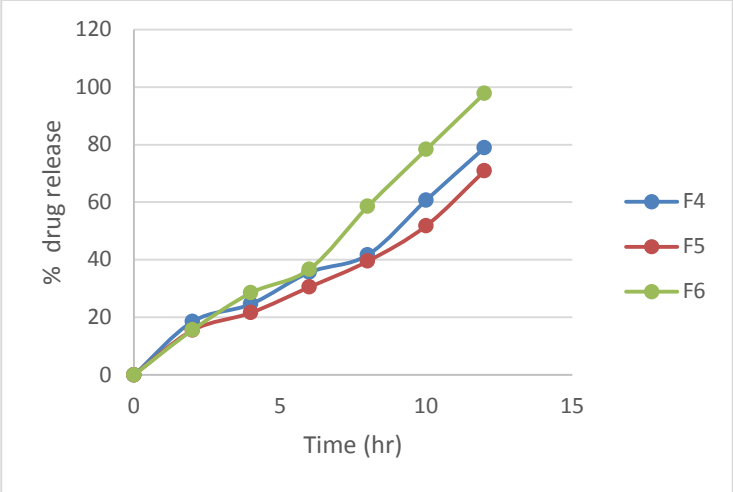


Figure 5: Percentage drug release (F4-F6)

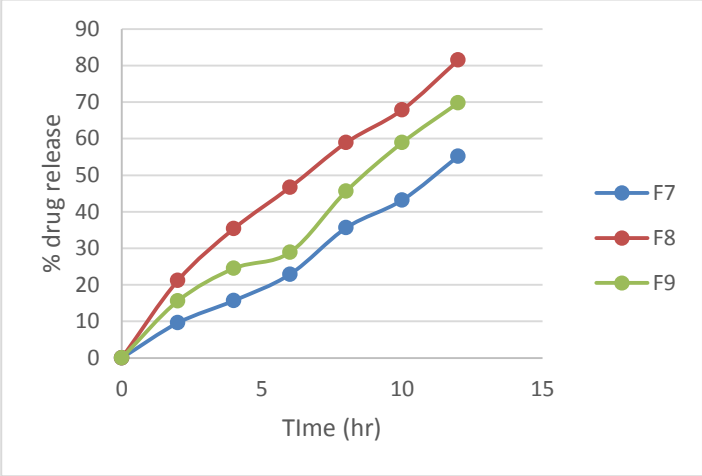


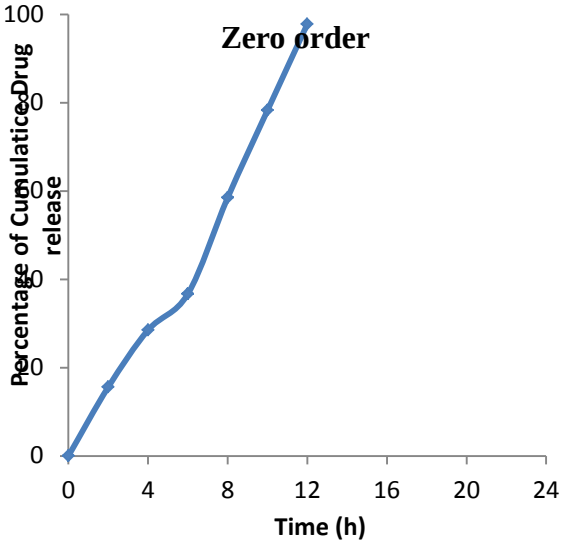
Figure 6: Percentage drug release (F7-F9)

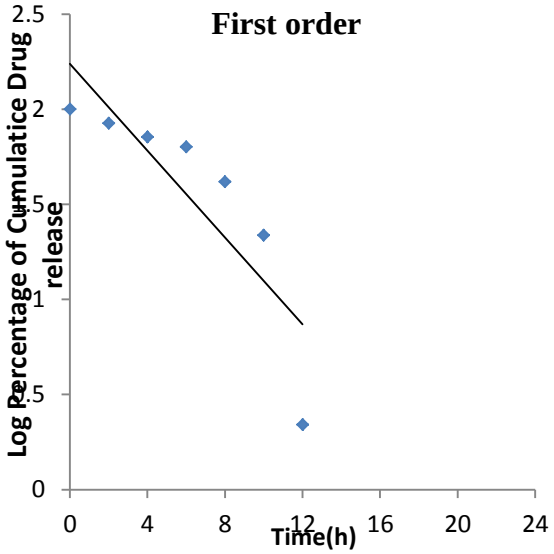
Kinetic Analysis of Dissolution Data

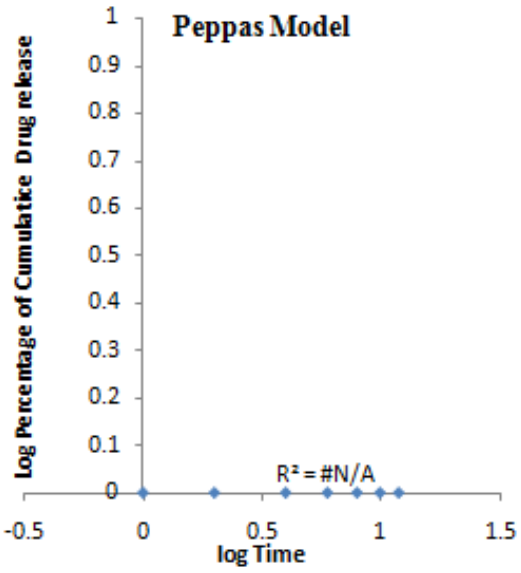
To analyse the drug release mechanism the invitro release data was fitted into various release equations and kinetic models zero order, first order, Higuchi and Korsmeyer Peppas model. The releasekinetics of Optimized formulation is shown.

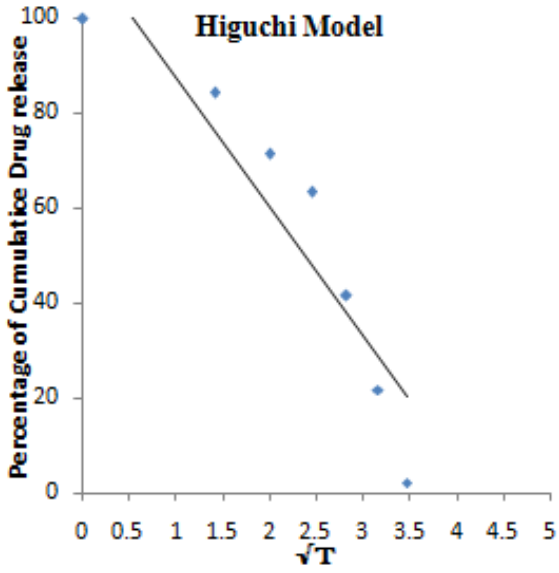
Table 6: Kinetic release of the drug

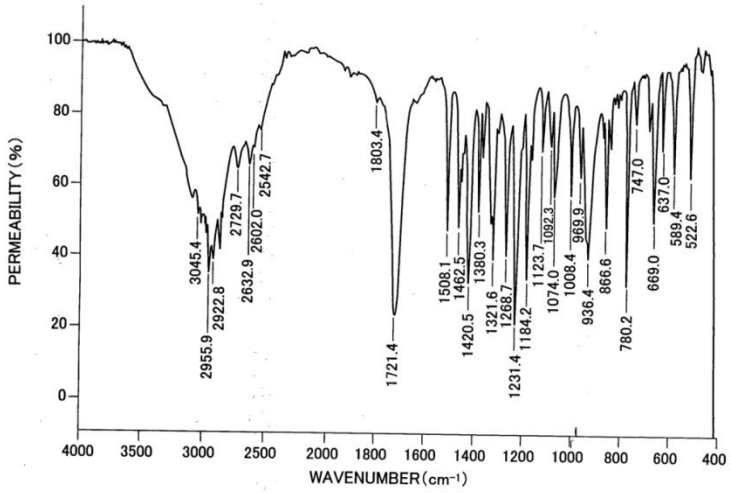
Formulation code	Zero order	First order	Higuchi	Peppas	
	R2	R2	R2	R2	N
F6	0.98	0.73	0.86	0.98	1.02


Zero order
Percentage of Cumulatice Drug release
Time (h)
0
20
40
60
80
100
0
4
8
12
16
20
24


First order
Log Percentage of Cumulatice Drug release
Time(h)
0
0.5
1
1.5
2
2.5
0
4
8
12
16
20
24


Peppas Model
Log Percentage of Cumulatice Drug release
log Time
R² = #N/A
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
-0.5
0
0.5
1
1.5


Higuchi Model
Percentage of Cumulatice Drug release
√T
0
20
40
60
80
100
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5



The present investigation was under taken to formulate and Controlled release tablets of Levofloxacin.

Sustain release Tablets

Using various polymers like Guar gum, Xanthum gum and HPMC K100, tablets were prepared along with other additives. Melt granulation method was used for the preparation of tablets. A total number of 9 formulations were prepared and evaluated.

Pre compressional studies

The results obtained by evaluating the powder blends of drug and excipients. Bulk density and tapped density were found in the range 0.52-0.56 g/cc and 0.62-0.69 g/cc respectively. The value of hausner's ratio was in between 1.16-1.25 (< 1.3) indicating that all batches of powder blends were having good compressibility. Values of angle of repose (θ) was found in the range of 19.65-25.8 showing that blend of powder mass was Good flowing.

Weight variation and Thickness

In vitro dissolution

In vitro dissolution studies are performed for Sustained tablets of Levofloxacin mixture of solvent 0.1N hcl using USP dissolution apparatus type 2. The dissolution rate was found to increase linearly with increasing concentration of polymer. The optimized formulations are Guar gum containing tablets (F6).Formulation have recorded drug 98.8respectively in 12 hrs.

Drug Release Kinetics

In vitro drug release data of all the Sustained formulations was subjected to goodness of fit test by linear regression analysis according to zero order and first order kinetic equations, Higuchi's and Korsmeyer–Peppas models to ascertain the mechanism of drug release.

CONCLUSION

The primordial aim of formulating levofloxacin controlled release tablets has been accomplished well indeed. The *In-vitro* drug release study recommends the product for further *in vivo* studies, which may improve patient compliance. From the results, formulationf6 containing Levofloxacin 250 mg, Xanthum gum evolved as the optimized formulation and it releases more than 97.8% drug in 12hrs. The optimized formulation would be a promising Sustained drug delivery system of Levofloxacin providing nearly zero order drug release over a period of 12 hrs.

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REFERENCES

[1]. Beckett AH, Stenlake JB, Practical Pharmaceutical Chemistry. Delhi: CBS Publisher and Distributors, 4, 1997.

[2]. P D Sethi, Quantitative Analysis of Drugs in Pharmaceutical Formulation, 3rded. Delhi: CBS Publisher and Distributors.

[3]. P D Sethi, High Performance Liquid Chromatography, Delhi: CBS Publisher and Distributors.

[4]. Higuchi T andbrochman E, Hanseen H, Pharmaceutical Analysis, Delhi: CBS Publisher and Distributors, 2005.

[5]. Mendham J, Denney RC, Barnes JD, Kthomas MJ, Vogel's text Book of Quantitative Chemical Analysis,. Pearson education Pvt Ltd, 6, 2002.

[6]. Anderson NR et al., Quantitative evaluation of pharmaceutical effervescent systems I: design of testing apparatus. J Pharm. Sci. 71(1), 1982, 3-6.

[7]. Barra J, Somma R., Influence of the physicochemical variability of magnesium stearate on its lubricant properties: possible solutions. Drug devind Pharm. 22(11), 1996, 1105-1120.

[8]. Billanymr, Richards JH..Batch variation of magnesium stearate and its effect on the dissolution rate of salicylic acid from solid dosage forms. Drug devind Pharm.8, 1982, 497-511.

[9]. Bosceetal., Lubricant sensitivity in relation to bulk density for granulations based on starch or cellulose. Int J Pharm.67, 1991, 39-49.

[10]. Bracconi P et al. Structural properties of magnesium stearate pseudopolymorphs: effect of temperature. Int J Pharm. 262(1–2), 2003, 109-124.

[11]. Brittainhg. Raw materials. Drug devind Pharm. 15(13), 1997, 2083-2103.

[12]. Dansereau R., Peck GE., The effect of the variability in the physical andchemical properties of magnesium stearate on the properties of compressed tablets. Drug devind Pharm.13, 1987, 975–999.

[13]. Desai dsetal.,. Physical interactions of magnesium stearate with starch-derived disintegrants and their effects on capsule and tablet dissolution. Int. J. Pharm. 91(2–3), 1993, 217-226.

[14]. Ebbafetal.,. Stress relaxation studies of granules as a function of differentlubricants. Eur. J. Pharm. Biopharm. 52(2), 2001, 211–220.

[15]. Frattini C, Simioni L., Should magnesium stearate be assessed in theformulation of solid dosage forms by weight or by surface area. Drug devind Pharm.10, 1984, 1117-1130.

[16]. He Xetal. Mechanistic study of the effect of roller compaction andlubricant on tablet mechanical strength. J Pharm Sci. 96(5), 2007, 1342-1355.

[17]. Javaid KA, Cadwallader DE. Dissolution of aspirin from tablets containing various buffering agents. J Pharm. Sci. 61(9), 1972, 1370-1373.

[18]. Koivistometal Effect of temperature and humidity on vegetable grade magnesiumstearate. Powder), 2004, 79-85.

[19]. Leinonenuiet al., Physical and lubrication properties of magnesiumstearate. J Pharm.Sci. 81(12), 1992, 1194-1198.

[20]. Likitlersuang Set al. The effect of binary mixture composition and magnesium stearate concentration on the hiestand tableting indices and other related mechanical properties. Pharm.Dev Technol. 12(5), 2007, 533-541.

[21]. Marwaha SB, Rubinstein MH Structure-lubricity evaluation of magnesium stearate. Int J Pharm. 43(3), 1988, 249-255.