Pamula Reddy Bhavanam et al, /J. Pharm. Sci. & Res. Vol.2(5), 2010, 308-313

ISSN:0975-1459

Journal of Pharmaceutical Sciences and Research

www.jpsr.pharmainfo.in

Formulation and Evaluation of Levofloxacin Using Different Types and Concentrations of Superdisintegrants

Pamula Reddy Bhavanam*, Vamshi Krishna Lekkala, Priyanka Maddirala, S. Narender Reddy, A. Sai Krishna, CH. Rajesh

Department of Pharmaceutics, Vishnu Institute of Pharmaceutical Education And Research, Vishnupur, Narsapur, Medak (Dist), Andhra Pradesh, India-502313.

Abstract:

Levofloxacin is a fluoroquinolone anti bacterial drug effective in the treatment of bacterial conjunctivitis**.** Levofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class. The objective of the present work was to comparison of super disintegrants on Levofloxacin oral formulations. Levofloxacin oral formulations were prepared with different concentrations (5%, 10%), of each super disintegrants. The super integrants were sodium starch glycolate (SSG), crosspovidone (XL-10) and crosscarmellose sodium (CCS) used in the preparation of Levofloxacin oral formulations. The formulations were coded as Lev1 (SSG), Lev2 (Cross povidone) and Lev3 (CCS). The Levofloxacin oral formulation (Lev2) with cross povidone (XL-10) 10% has shown the better disintegration time and increases the dissolution rate when compared to the other super disintegrants.

***Keywords*:** Levofloxacin, In vitro study, Release kinetics.

Introduction:

Levofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class [1, 2] and is used to treat severe or life-threatening bacterial infections or bacterial infections which have failed to respond to other antibiotic classes [3, 4]. Levofloxacin is also marketed worldwide for oral and IV use, as well as used in ophthalmic solutions. Levofloxacin chemical name is (-)-(S)-9-fluoro-2, 3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7Hpyrido [1, 2, 3-de]-1, 4 benzoxazine-6-carboxylic acid hemihydrate. Levofloxacin is a chiral fluorinated carboxyquinolone. Investigation of ofloxacin, an older drug that is the racemic mixture, found that the l form [the (–)-(*S*) enantiomer] is more active. This specific component is Levofloxacin [5, 6].

Levofloxacin interacts with a number of other drugs, as well as a number of herbal and natural supplements. Such interactions increase the risk of cardiotoxicity and arrhythmias, anticoagulation, the formation of non-absorbable complexes, as well as increasing the risk of toxicity [7].

Levofloxacin is associated with a number of serious and life-threatening adverse reactions as well as spontaneous tendon ruptures and irreversible peripheral neuropathy. Such reactions may manifest long after therapy had been completed and in severe cases may result in life long disabilities. Hepatoxicity has also been reported with the use of Levofloxacin [8, 9]. Levofloxacin has shown moderate activity against anaerobes, and is about twice as potent as ofloxacin against mycobacterium tuberculosis and other mycobacteria, including mycobacterium avium complex [10].

Levofloxacin has been reported to interact with a significant number of other drugs, as well as a number of herbal and natural supplements. Such interactions increased the risk of cardiotoxicity and arrhythmias, anticoagulant effects, the formation of non-absorbable complexes, as well as increasing the risk of toxicity.

Some drug interactions are associated with molecular structural modifications of the uinolone ring, specifically interactions involving NSAIDS and theophylline. The fluoroquinolones have also been shown to interfere with the metabolism of caffeine [11] and the absorption of levothyroxine. The interference with the metabolism of caffeine may lead to the reduced clearance of caffeine and a prolongation of its serum half-life, resulting in a caffeine overdose. Ciprofloxacin has been shown to interact with thyroid medications (levothyroxine) resulting in unexplained hypothyroidism [12]. As such it is possible that levofloxacin may interact with thyroid medications as well.

Materials and Methods:

Levofloxacin was obtained as a complimentary sample from MSN Laboratories Ltd, Hyderabad. SSG, Cross povidone and CCS were purchased from YARROW chemicals Ltd, Mumbai. Magnesium Stearate, Lactose mono hydrate was purchased from vijaya Scientifics, Hyderabad.

Preparation of Levofloxacin Tablets

Tablets were prepared by wet granulation method. Levofloxacin, Lactose monohydrate, and super disintegrant was weighed accurately and sieved through #20. . Hpc was used as a binder solution for granulation. Hpc was dissolved in sufficient quantity of water. The dry mix was granulated using Hpc binder solution. The wet granule obtained from granular was passed through 10# and wet granules were dried in hot air oven at 50 c. The dried granules were sifted through 20# were lubricated with magnesium Stearate and anhydrous lactose. Lubricated granules were compressed using single punch machine.

Dissolution test

Dissolution rate of Levofloxacin tablets was studied using USP II (paddle Type) dissolution test apparatus. The quantity of dissolution medium was 900 ml of 0.1N HCL, with the speed of rotation at 100 rpm and the temperature was set at 37+ 0.5 c. The sample was withdrawn at different time intervals. The withdrawn samples were suitably diluted with more quantity of dissolution medium and the same volume was replaced with fresh dissolution medium. The samples were then studied in UV spectrophotometer at281 nm for Levofloxacin content. The release rate at different time intervals were then determined.

Results and Discussion:

Levofloxacin oral formulation with different types and concentrations of super disintegrants were subjected for disintegration test and dissolution test. The levofloxacin oral formulations were prepared with different types and a concentration of super disintegrates. The disintegration time of each levofloxacin oral formulations were observed. Among all the three formulations (Lev 1, Lev 2, Lev 3), Lev 2 (10%) has shown the better disintegration time.

Table 1: Composition of Levofloxacin Oral Formulations

S.NO.	Ingredients	Lev 1(mg/tab)		Lev 2(mg/tab)		Lev 3(mg/tab)	
		5%	10%	5%	10%	5%	10%
1	Levofloxacin	250	250	250	250	250	250
2	Lactose monohydrate	185	170	185	170	185	170
3	SSG	25	50	-	-	-	-
4	Cross Povidone (XL-10)	-	-	25	50	-	-
5	CCS	-	-	-	-	25	50
6	Hpc (EXF)	15	10	15	10	15	10
7	Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
8	Anhydrous lactose	20	15	20	15	20	15
9	Magnesium Stearate	5	5	5	5	5	5

Table 2: Disintegration profile for Levofloxacin oral formulation

S.No.	Concentration	Disintegration Time (Mins)		
		Lev 1	Lev 2	Lev 3
1	5%	15	10	14
2	10%	9	6	10

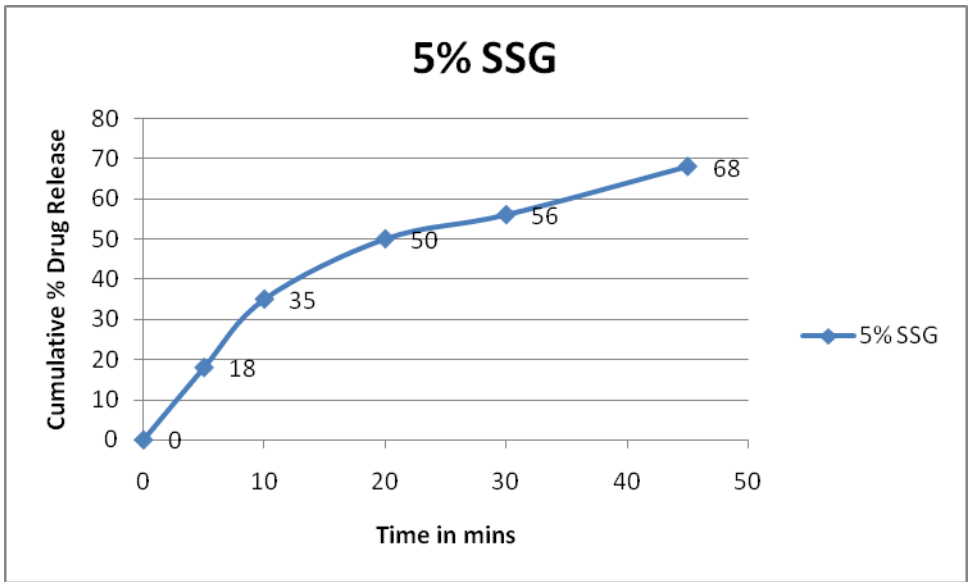

Fig 1: In-vitro dissolution studies of Lev 1 formulation with 5% SSG

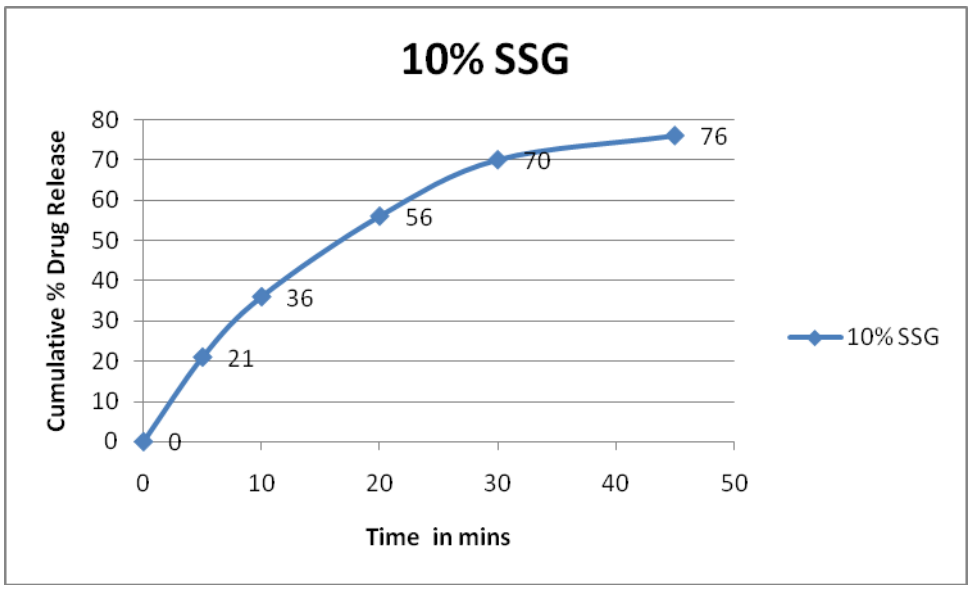

Fig 2: In-vitro dissolution studies of Lev 1 formulation with 10% SSG

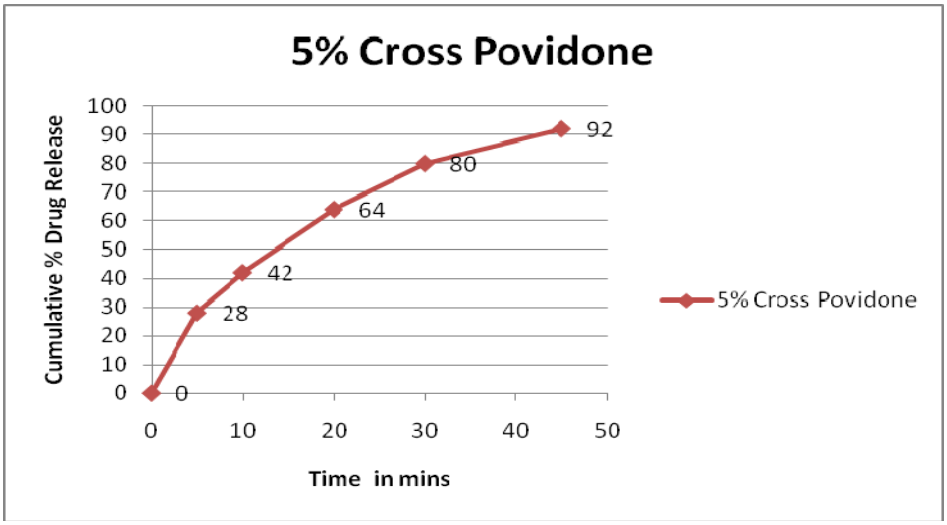

Fig 3: In-vitro dissolution studies of Lev 2 formulation with 5% cross povidone (XL-10)

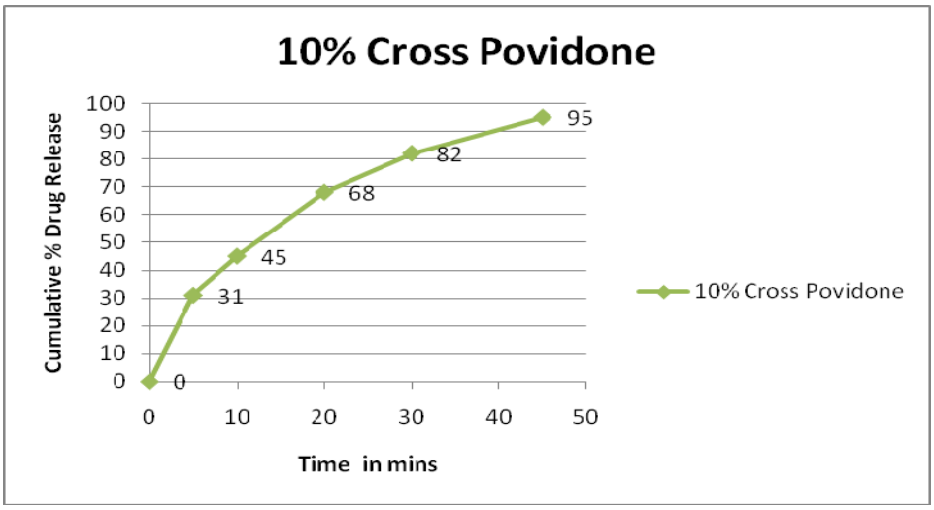

Fig 4: In-vitro dissolution studies of Lev 2 formulation with 10% cross povidone (XL-10)

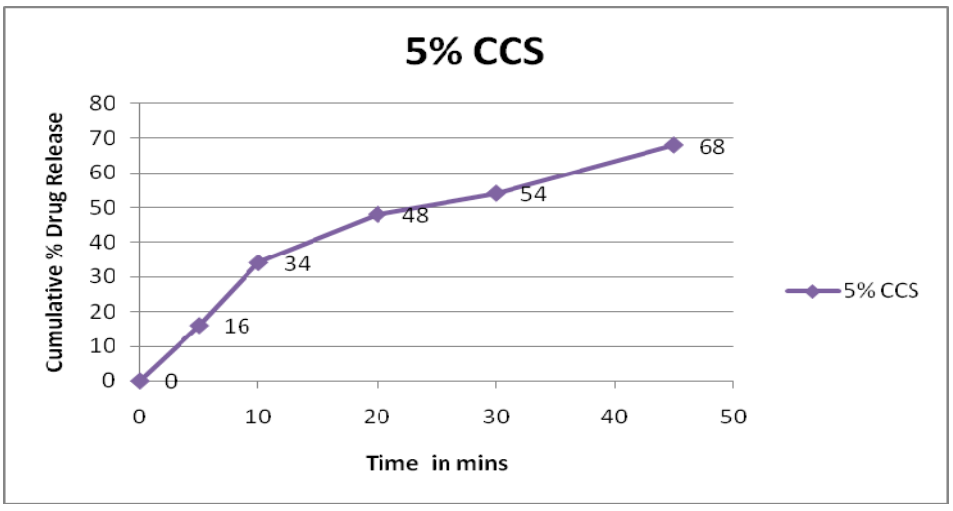

Fig 5: In-vitro dissolution studies of Lev 3 formulation with 5% CCS

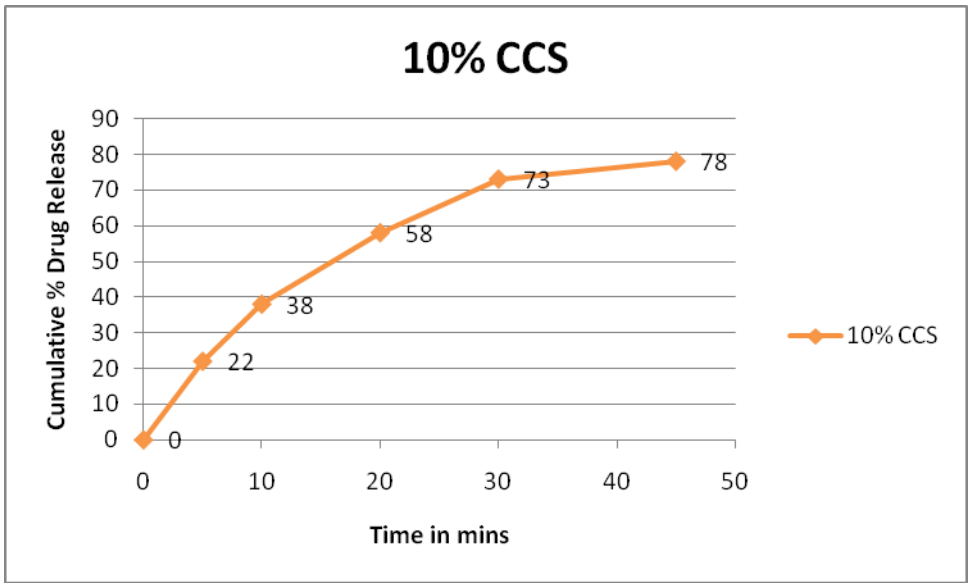

Fig 6: In-vitro dissolution studies of Lev 3 formulation with 10% CCS

Conclusion:

Levofloxacin tablets containing different types and concentrations (5%, 10%) of super disintegrants (SSG, CCS and Cross povidone XL-10) were prepared by wet granulation method and subjected to disintegration studies and in vitro drug release studies. The disintegration time for three formulations was observed. Lev 2 shows the better disintegration than the Lev1 and Lev 3. The disintegration time for Lev 2 (5%) is 10mins and (10%) is 6mins. In -vitro dissolution profile is also shows that Lev 2 has the better percentage drug release when compared to the Lev 1 and Lev 3. The levofloxacin formulation Lev 2 (Cross povidone XL-10) with 5% super disintegrant the % of release was found to be 92% and levofloxacin formulation Lev 2 (Cross povidone XL-10) with 10% super disintegrant the % of release was found to be 95%. The Levofloxacin oral formulation Lev 2(Cross povidone XL-10) with 5%, 10% shows the better disintegration time and % of drug release.

Acknowledgements:

The authors are thankful to our chairman Sri K V Vishnu Raju for supporting us in every aspect to develop the Research work**.** The authors are also grateful to Dr. V.H.K. Verma, principal and staff Vishnu Institute of Pharmaceutical Education & Research, Narsapur, Medak, Andhra Pradesh. They are also thankful to MSN laboratories Ltd, Hyderabad for providing free gift sample.

References:

[1] Nelson, JM.; Chiller, TM.; Powers, JH.; Angulo, FJ. (Apr 2007). "Fluoroquinolone-resistant Campylobacter species and the withdrawal of fluoroquinolones from use in poultry: a public health success story.". *Clin Infect Dis* 44 (7): 977-80. doi:10.1086/512369. PMID 17342653.

[2] Kawahara, S. (Dec 1998). "[Chemotherapeutic agents under study]". *Nippon Rinsho* **56** (12): 3096-9. PMID 9883617.

[3] Liu, H.; Mulholland, SG. (July 2005). "Appropriate antibiotic treatment of genitourinary infections in hospitalized patients.". *Am J Med* 118 Suppl 7A: 14S-20S. doi:10.1016/j.amjmed.2005.05.009. PMID 15993673.

[4] MacDougall C, Guglielmo BJ, Maselli J, Gonzales R (March 2005). "Antimicrobial drug prescribing for pneumonia in ambulatory care". *Emerging Infect. Dis.* 11 (3): 380–4. PMID 15757551.

[5] Janssen Pharmaceutica (September 2008). "HIGHLIGHTS OF PRESCRIBING INFORMATION" . USA: FDA.

[6] Morrissey, I.; Hoshino, K.; Sato, K.; Yoshida, A.; Hayakawa, I.; Bures, MG.; Shen, LL. (August 1996). "Mechanism of differential activities of ofloxacin enantiomers." .

Antimicrob Agents Chemother 40 (8): 1775–84. PMID 8843280. PMC 163416.

[7] Drug Bank. "Showing drug card for Levofloxacin (DB01137)". Canada. http://www.drugbank.ca/drugs/DB01137.

[8] Renata Albrecht "NDA 20-634/S-045, NDA 20-635/S-048, NDA 21-721/S-013" (PDF). USA: http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2007/020634s045,%20020635s048,%20021721s013ltr.pdf.

[9] Renata Albrecht "NDA 20-634/S-051, NDA 20-635/S-055, NDA 21-721/S-019" (PDF). USA:FDA..http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2008/020634s051,%20020635s055,%20021721s019ltr.pdf.

[10] John A. Bosso (1998). "New and Emerging Quinolone Antibiotics". *Journal of Infectious Disease Pharmacotherapy* 2 (4): 61–76. doi:10.1300/J100v02n04_06. ISSN 1068-7777.

[11] Harder S, Fuhr U, Staib AH, Wolff T (November 1989). "Ciprofloxacin-caffeine: a drug interaction established using in vivo and in vitro investigations". *Am. J. Med.* 87 (5A): 89S–91S.

[12] Cooper JG, Harboe K, Frost SK, Skadberg Ø (April 2005). "Ciprofloxacin interacts with thyroid replacement therapy". *BMJ* 330 (7498):1002. doi:10.1136/bmj.330.7498.1002. PMID 15860826. PMC 557149.