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RESEARCH ARTICLE

ACCELERATED STABILITY STUDIES OF FLURBIPROFEN FILM COATED TABLETS OF FIVE DIFFERENT NATIONAL BRANDS IN PAKISTAN

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ABSTRACT

Flurbiprofen is a potent non-steroidal anti-inflammatory drug, prescribed commonly for musculoskeletal and joint disorders like arthritis. It is well established that drug degradation during storage and transportation is of particular issue in tropical countries like Pakistan, having areas with temperature variations from 0°C (Muree, Islamabad, Sawat and Azad Jammu Kashmir) to 50°C (Sibi, Jackababad, Nawabshah, Larkana, Multan and Bahawalpur) and some areas with high relative humidity (Karachi). Present study was designed to evaluate five different national brands of flurbiprofen 100 mg film coated tablets by accelerated stability studies and examined for the parameters of hardness, disintegration, dissolution and assay for drug concentration in formulation after one, three and six months duration at controlled tropical conditions of temperature and relative humidity. Dosage forms of all selected national brands were found stable even after expiry date.
Keywords: Flurbiprofen, Accelerated stability study, Dissolution, Disintegration, Assay

INTRODUCTION

Stability of pharmaceutical products is important for patient's safety[1] and stability calculations of expiration date of the product[2]. Stability of pharmaceutical product means the physical and chemical integrity of dosage form and its ability to guard against microbial contamination[3]. Pharmaceutical products adopt various pathways of chemical degradation including hydrolysis, oxidation, deamination and cyclization[4]. Accelerated stability studies are performed in order to predict the long term stability of pharmaceutical products[5]. They also help to identify the major degradation products; degradation pathways and stability indicating potential of analytical procedure used[6].These studies are performed by exposing the representative sample of pharmaceutical product to stress conditions of temperature, humidity, light and radiations. Most companies conduct some types of accelerated degradation studies but companies' practices vary widely in term of when and how these studies are to performed[8]. Flurbiprofen is a chiral, 2-arylpropionic acid derived non-steroidal anti inflammatory drug having potent cyclooxegenase non selective inhibition activity[8], shorter biological half-life and stereoselective pharmacokinetics[9]. It is used for the treatment of musculoskeletal and joint disorders like arthritis and acute gout. Film coated flurbiprofen tablets are elegant in appearance and improved gastric tolerability[11].

The aim of this study was to conduct accelerated stability studies of 100mg film coated flurbiprofen tablets from different national brands in Pakistan in order to evaluate the parameters of dissolution, disintegration, hardness and drug potency (WHO guidelines for stability testing, 2006)[11] at different time intervals of 1, 3 and 6 months as function of temperature and relative humidity at tropical conditions according to ICH guidelines, 2003.

MATERIALS AND METHODS

Flurbiprofen 100 mg film coated tablets, which were 5 months near to their expiration date, of five different national brands i.e. Flurbin®, Rubinol®, Flurle®, Frugesic®, Eyeflox® were collected randomly from Mass pharma (Pvt) Ltd. Lahore, Obsons Pharmaceuticals (Pvt) Ltd. Lahore, Leads Pharma (Pvt) Ltd. Islamabad, Mediceena Pharma (Pvt) Ltd. Lahore, P.D.H Pharmaceuticals (Pvt) Ltd. Lahore respectively. Hardness tests were performed on MH-1 Galvano Scientific while for disintegration and dissolution tests, basket-rack assembly USP 30 (Galvano Scientific) and six stations USP 30 type II paddle apparatus (Galvano Scientific) were used respectively. Assay for concentration of flurbiprofen was performed on Optizen 2010 UV and was also determined by titrometric analysis. All other chemicals used were of analytical grade and were used without any chemical modification.

Accelerated Stability Studies

Flurbiprofen 100mg film coated tablets in form of packs in triplets were placed in stability chamber with controlled temperature and humidity of class IV climatic conditions as recommended by ICH guidelines 2007. Temperature was maintained at 40 ± 2°C and relative humidity was controlled by KCI solution at RH 75±5 %.

Tablet hardness

Hardness of tablets was determined by placing them in plungers of Hardness Tester, measuring the average force in Kilogram by triplicate of tests.

Disintegration studies

Disintegration studies were performed according to USP 30 specifications. Six tablets were placed in basket rack assembly of apparatus. Basket was moved with frequency

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of 29 to 32 cycles per minute in distilled water, maintained at 37 ± 2°C.

Dissolution studies

In vitro drug release studies were performed by dissolution test USP 30 for 6 hours, using phosphate buffer at pH of 7.20 ± 0.05 maintained at 37 ± 2°C as dissolution medium for film coated tablet and measuring the absorbance at 247nm at UV visible spectrophotometer. Sample of 5ml was first taken after 45 minutes and then after every 30 minutes and replaced by fresh dissolution medium to maintain the volume. Concentration of drug in sample was measured, after filtration and dilution, by calibration curves and percentage drug release was calculated.

Assay

Assay was performed by two ways;

Titrimetric Analysis

20 tablets were crushed and powdered. Powder weighing equivalent to 200 mg flurbiprofen was dissolved in 50 ml (96%) methanol. This solution was titrated against 0.1M NaOH, determining end point potentiometrically. 1 ml of 0.1M of NaOH is equivalent to 24.43mg of $C_{15}H_{13}FO_2$[12].

Spectrophotometric analysis

Spectrophotometric analysis was performed on UV visible spectrophotometer. Standard was prepared of 0.01mg/ml by dissolving 100 mg of flurbiprofen in 100 ml of 0.01N NaOH and then diluting it. Sample solution was prepared by crushing and powdering 20 flurbiprofen tablets and dissolving powder weighing equivalent to 100 mg flurbiprofen in 100 ml of 0.01N NaOH and diluting upto 0.01mg/ml. Absorbance was measured at 247nm and percentage of flurbiprofen was determined as[13]

Percentage of flurbiprofen = (A sample ×100)/A standard

Where A is Absorbance. Acceptable limits were 90-110%.

Assay was performed as triplicate of both methods and drug concentration in tablet was measured as average.

RESULTS

Tablet hardness

Table 1: Hardness of different brands of flurbiprofen 100 mg film coated tablets

Brands	Hardness (average) (kg/cm²/tablet)		
	One month	Three month	Six month
Flurbin	7.6	7.5	7.1
Rubinol	7.3	7.2	6.5
Flurle	8.1	7.7	6.9
Frugesic	7.8	7.5	6.8
Eyeflox	8.5	8.1	7.2

Disintegration studies

Table 2: Results of disintegration studies of different brands of flurbiprofen 100 mg film coated tablets

Brands	Disintegration time (average) (min)		
	One month	Three month	Six month
Flurbin	8.10	7.95	7.10
Rubinol	8.21	8.13	7.25
Flurle	8.61	8.43	7.80
Frugesic	8.95	8.65	8.15
Eyeflox	8.25	8.05	7.88

Dissolution studies

Table 3: Results of dissolution studies of different brands of flurbiprofen 100mg film coated tablets

Brands	Dissolution (average) (%age)		
	One month	Three month	Six month
Flurbin	91.32	86.45	78.53
Rubinol	95.82	89.33	80.52
Flurle	99.24	92.52	77.83
Frugesic	90.40	83.53	76.85
Eyeflox	92.05	85.38	79.90

Assay

Table 4: Results of assays of different brands of flurbiprofen 100 mg film coated tablets

Brands	Assay (average) (%age)		
	One month	Three month	Six month
Flurbin	99.76	97.65	91.5
Rubinol	102.26	101.61	96.40
Flurle	98.62	98.33	92.53
Frugesic	95.39	94.99	90.81
Eyeflox	102.10	101.85	95.33

DISCUSSION

Flurbiprofen is a potent NSAID been in clinical use for many years. Formulation tests recommended in pharmacopoeia monographs are useful in determining in vivo efficacy. Hardness of tablets, after keeping in stability chamber for 6 months at controlled temperature and humidity was not significantly affected up to 3 months of studies as tablet gains moisture and its hardness increases then subsequently loose it[14] whereas hardness of all brands decreased after six months significantly. Disintegration and dissolution decreased in same manner during 6 months studies, under increased humidity. However difference of disintegration pattern from that of hardness can be justified due to excipients function[15]. Assay of five different brands was conducted by both spectrophotometer and titrimetric analysis, and results were calculated as average, and results were in the range of 90-110% USP 30 and there was no marked effect on assay of brands taken for studies.

From above discussed data, flurbiprofen film coated tablets of all national brands have been found stable even after expiry date. Therefore, it has been concluded that stability study of flurbiprofen found equally accurate, reproducible, robust, and could be applied directly and easily to the pharmaceutical preparations of flurbiprofen. However excipients function was not taken into account which can impart deviation from above results.

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