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Original Article

Degradation Study of Meloxicam by UV Spectroscopy

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A B S T R A C T

Objective: The aim of this study was to perform the forced degradation studies i.e. the effect of heat, UV light, acid and base on different brands of meloxicam as defined under ICH guideline Q1A (R2) by using spectrophotometer.

Methodology: The degradation studies were carried out by preparing the standard solution of 200ppm of each brand of meloxicam .The working solutions were prepared from the standard solution and by the addition of 0.1 N HCl , 0.1 N NaOH and de-ionized water in separate test tube. The detection of the effect of acid and base were performed by placing the test tubes of solution of each brand at room temperature and the effect of UV and heat were performed by leaving the test tubes of solution at 320 nm and 50°C respectively.

Result: The result of this study illustrated that when different brands of meloxicam (A, B and C) were introduced in 0.1 N NaOH (basic medium) less degradation was observed in brand A and B while significant degradation was observed in brand C . When different brands of meloxicam (A, B and C) were introduced in 0.1 N HCl (acidic medium) the two brands B and C showed significant degradation while brand A showed highly significant degradation. Whereas when the different brands (A, B and C) were exposed to Ultraviolet light (320 nm) for 30 min, all of three brands A, B and C showed significant degradation. When different brands (A, B and C) were exposed to heat (50°C), brand A, B and C showed significant degradation after different time interval (0, 10, 20, 30, 40, 50 and 60 minutes).

Conclusion: The UV spectroscopy analysis of amount of degraded product is usually preferred over other methods because of less equipment cost and economical maintenance advantage. It is easy and rapid method and can be use in routine detection in QC laboratories.

Keywords: Meloxicam, UV spectroscopy, Forced degradation, Different brands and ICH guideline.

INTRODUCTION

Meloxicam (fig. 1) is chemically known as 4-hydroxy-2 methyl- ({N-[5-methyl-2-thiazolyl]-2H-1}, 2-benzothiazine-3-carboxamide-1, [1-dioxide]). It is a non steroidal anti-inflammatory drug (NSAID) which belongs to the oxicam class. It is used to relieve the symptoms of pyrexia, primary dysmenorrhea, arthritis, and as an analgesic, especially where there is an inflammatory element[1,2]. Meloxicam inhibits the synthesis of enzyme cyclooxygenase (COX) that is responsible for converting the arachidonic acid into prostaglandin H_2. This conversion is the first step in the synthesis of mediators of inflammatory i.e. prostaglandins. Meloxicam especially at its low therapeutic dosage selectively inhibit cyclooxygenase-2 (COX-2) over cyclooxygenase-1 (COX-1) without affecting platelet aggregation[3-5]. The poor water solubility (0.012 mg/ml) of meloxicam strongly limited the therapeutic efficacy[6]. The principal advantage of meloxicam which permits one daily dosing is high degree of enterohepatic circulation and longer half life (15- 20 hrs) aside from low aqueous solubility[7,8]. The lower dose of meloxicam (7.5mg/day) is usually prescribed in gastric disease. Meloxicam is safer than other NSAID's though prolonged use of the drug is associated with gastro-intestinal side effects such as flatulence, abdominal pain, gastric and duodenal ulcers, nausea, diarrhea[9,10]. (See figure 1.)

Spectrophotometric technique is based on measuring the absorption of a monochromatic light in the near ultraviolet region (200-380 nm). UV spectro-photometer can also be use for stress degradation studies. According to International Conference of Harmonization (ICH) guideline the active pharmaceutical ingredient is focused to various forced degradation conditions[12] which involve temperature humidity, acid and base stress testing, high and low pH variation, photo degradation and time. Thermal with or without humidity stress testing is performed by exposing the drug substance to thermal/humidity conditions in due course which causes the substance to degrade forcefully to its main components. UV degradation is a main problem in numerous UV-unstable products which are made up of natural and synthetic polymers as they break or disintegrate when exposed to constant sunlight. The attack is dependent on the degree of exposure as the nonstop exposure is a major problem than intermittent exposure. Acid/base forced degradation testing is used for the evaluation of degradation of a drug substance by exposure to basic or acidic medium over time to its primary degradation products. Acid/base hydrolysis takes place in labile carbonyl functional groups for e.g. Alcohols, imines, imides amides (lactams), esters (lactones), aryl amines, and carbamates. Forced degradation is capable of demonstrating that the preferred technique is stability indicating and this technique use to identify the raise in the degradation product and the subsequent loss of active constituent[13-15]. The aim of the study is to perform forced degradation studies of the different brands of meloxicam under hydrolytic (acidic and basic), photolytic and thermal stress conditions, as defined under ICH guideline Q1A (R2) by using spectrophotometer. It is usually preferred over other methods because of less equipment cost and economical maintenance advantage[17-21].

EXPERIMENTAL

Material and reagents

All the glass materials used in this research were of Pyrex glass including stirrer, measuring cylinder, volumetric flask, pipette and funnel. Glass wares were initially washed by Chromic acid than rinse

with water and finally with DI water or double distilled water which was freshly prepared. All the reagents used in the working were of analytical grade including Hydrochloric acid (0.1N), Sodium hydroxide (0.1N) and DI water or double distilled water. The active use was in the form of different brands of meloxicam[16].

Instruments

1. Weighing Balance of Pioneer OHAIUS (Item PA214C),
2. Water Bath with 'HH-4' (DGT and CNST temperature tank.)
3. UV-VIS Spectrophotometer, 'PG Instrument', with a quartz cuvette.

Preparation of 0.1 N sodium hydroxide and hydrochloric acid

Analytical grade (37% purity and 12N normality) HCl was utilized for the preparation of 0.1 N HCl which was carried out by taking small quantity of water in a100 ml volumetric flask and transferring 8.36ml of hydrochloric acid in a flask and make up the final volume upto the mark with de-ionized (DI) water. The preparation of 0.1 N NaOH was carried out by weighing 4 grams of sodium hydroxide and transfer it in 100ml volumetric flask. Firstly take small portion of water and dissolve NaOH in it. Finally make up the volume with de-ionized water up to the mark of the flask.

Preparation of meloxicam solution of different brands

Separately weigh each tablet of three brands of meloxicam. Ground and triturate the tablets separately with the help of mortar pestle for each brand to convert them into powder form. Accurately weighed triturated powder equivalent to 20 mg of meloxicam in a tared beaker for each brand i.e. MILT3, MOBIC MELFAX and dissolve them in small quantity of DI water for making primary solutions of meloxicam and shake. The dissolved solutions were transferred into three different 100ml volumetric flasks. Lastly make-up the ultimate volume with de-ionized water to 100 ml for each sample. By using UV-Visible spectrophotometer, the absorbance of solutions of each brand of meloxicam (200ppm) was determined at wavelength max of 260nm.

Procedure for degradation Studies

The degradation studies were carried out by determining the effect of heat, UV acid and base on solution of three brands of meloxicam .The effect of heat and UV light on MILT3 (A), MOBIC (B) MELFAX (C) were determine by transferring 5 ml solution (200ppm) of each brand A, B and C in the six different test tubes each of the two test tubes contain same solution of each brand correspondingly then add 5 ml of de-ionized water in all of six test tubes. Now concentrations of the solution become 100ppm. Three test tubes containing solution of each brand A, B and C was kept in water bath at 50°C for 60 mins and another three test tubes containing solution of each brand was kept in Ultraviolet light for 30 mins at 320 nm. The effect of acid and base were determined by transferring 5 ml solution (200ppm) of each brand A, B and C in the six different test tubes each of the two test tubes contained solution of A, B and C brand correspondingly then add 5 ml of 0.1 N HCl solution in first set of three test tubes and 5 ml of 0.1 N NaOH solution in another set of three test tubes correspondingly. All the test tubes (12 test tubes) were left for 30 minutes. UV-Visible spectrophotometer was used for determining the absorbance of each solution at wavelength max of 260 nm.

RESULT AND DISCUSSION

We have conducted study on force degradation parameters of three different brands of meloxicam i.e. MILT3 (A),

MOBIC (B) MELFAX (C). Their absorbance for degradation parameters (acid, base and UV) before and after treatment demonstrated in Table 1 while parameter of heat (at different time interval) demonstrated in Table 2. The percentage of degradation of different brands of meloxicam is shown in Table 3 and 4 and their graphical representation is shown in Figure 2 and 3.

When 3 brands of meloxicam i.e. MILT3 (A), MOBIC (B) MELFAX (C) were subjected to 0.1 N NaOH, less changes in availability were observed in brand A (114.66%) and B (119.33%) while significant changes in availability was observed in brand C (164.26%) with respect to initial absorbance. When brands of meloxicam i.e. A, B and C are subjected to 0.1 N HCl, the two brands B and C showed significant changes in availability i.e. 54.89% and 49.72 % respectively while brand A showed highly significant changes in availability 23.32% with respect to initial absorbance. Similarly when different brands of meloxicam i.e. A, B and C were exposed to U.V light, all of the three brands A, B and C showed significant changes in availability i.e. 141.01% , 149.86% and 144.70% respectively . When the 3 brands A, B and C were subjected to heat (50°C) for 0, 10, 20, 30 ,40, 50 and 60 minutes, brand A shows slight changes in availability after heating for 0 min(137.05%), 10 min (135.78%), 20 min (139.13%) , 30 min(134.67%), 40 min (135.17%) , 50 min (134.67%) and 60 min (135.72%) . Brand B shows small changes in availability after heating for 0 min (128.73%), 10 min (134.94%), 20 min (139.13%), 30 min (137.56%), 40 min (136.50%), 50 min (136.56%) and 60 min (137.56%). Brand C shows changes in availability which increases gradually with time after heating for 0 min (130.33%), 10 min (135.96%), 20 min (139.18%), 30 min (140.25%), 40 min (138.50%), 50 min (139.01%) and 60 min (139.12%).

CONCLUSION

According to USP, meloxicam tablet contains not less than (NLT) 90.0 % and not more than (NMT) 110.0 % of the labeled amount of ($C_{14}H_{13}N_3O_4S_2$) meloxicam. The result of this study concludes that when chosen brands of meloxicam (A, B and C) were introduced in 0.1 N NaOH (basic medium) less degradation was observed in brand A and B while significant degradation was observed in brand C . When chosen brands of meloxicam (A, B and C) were introduced in the 0.1 N HCl (acidic medium) the two brands B and C showed significant degradation while brand A showed highly significant degradation. Whereas when the chosen brands (A, B and C) were exposed to Ultraviolet light (320 nm) for 30 min, all of the three brands A, B and C showed significant degradation .When chosen brands (A, B and C) were exposed to heat (50°C) for 30 min, brand A, B and C showed significant degradation after different time interval (0, 10, 20, 30, 40, 50 and 60 minutes). (See table 1 to 4 and figure 2&3.)

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Table 1. Absorbance of different brands of meloxicam

Parameters	Absorbance		
	MILT3	MOBIC	MELFAX
Before	1.814	1.789	1.774
Acid	0.423	0.982	0.882
Base	2.080	2.117	2.914
UV	2.558	2.681	2.567

Table 2. Absorbance of brands of meloxicam at different time interval

Heat	Absorbance		
Time interval (min)	MILT3	MOBIC	MELFAX
0	2.486	2.303	2.312
10	2.463	2.414	2.412
20	2.439	2.489	2.469
30	2.443	2.461	2.488
40	2.452	2.442	2.457
50	2.443	2.443	2.466
60	2.462	2.461	2.468

Table 3. Percentage of different brands of meloxicam

Parameters	Percentage of degradation		
	MILT3	MOBIC	MELFAX
Acid	23.32	54.89	49.72
Base	114.66	119.33	164.26
UV	141.01	149.86	144.70

Table 4. Percentage of different brands of meloxicam at different time interval

Heat	Percentage of degradation		
Time interval (min)	MILT3	MOBIC	MELFAX
0	137.05	128.73	130.33
10	135.78	134.94	135.96
20	139.13	139.13	139.18
30	134.67	137.56	140.25
40	135.17	136.50	138.50
50	134.67	136.56	139.01
60	135.72	137.56	139.12

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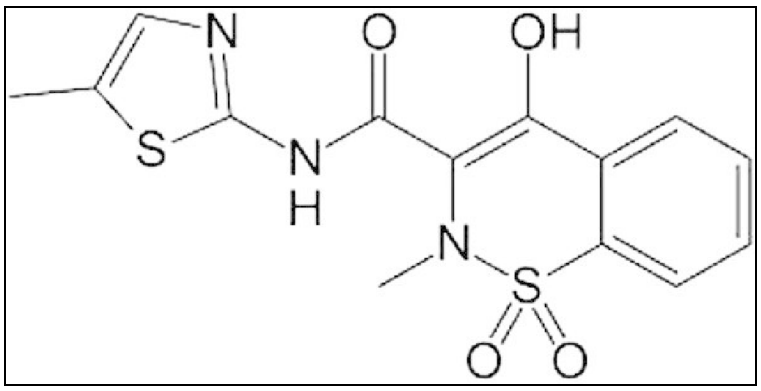

Figure 1. Structure of Meloxicam[11]

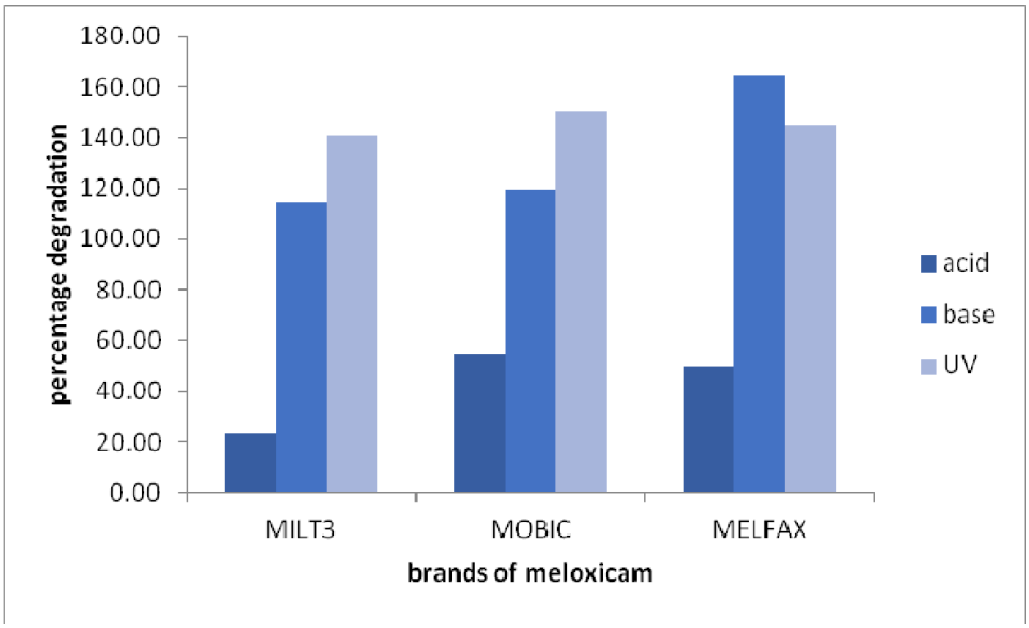

Figure 2. Degradation pattern of different brands of meloxicam

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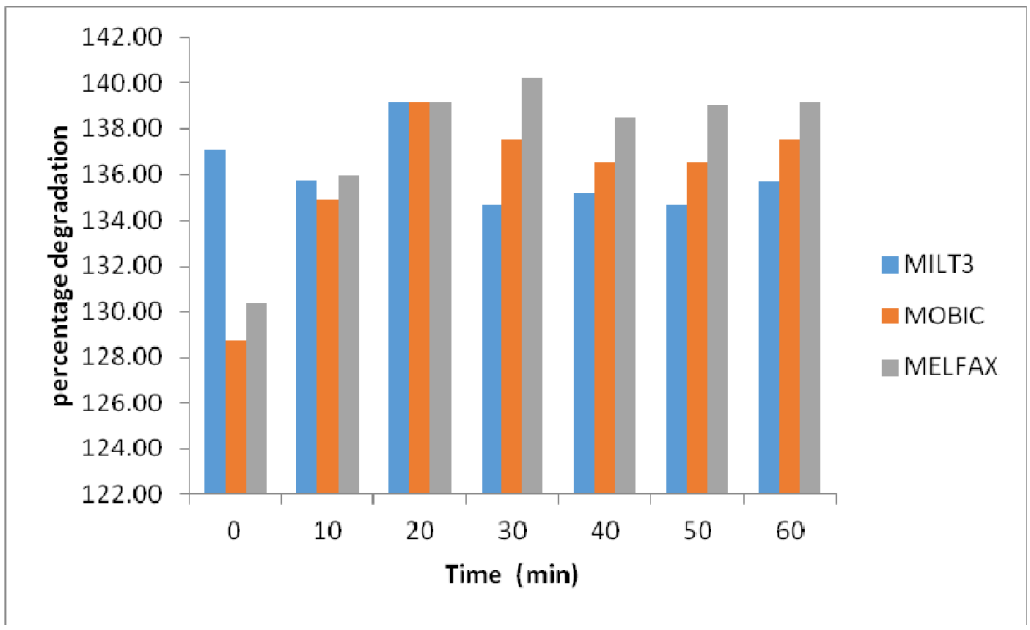

Figure 3. Degradation pattern of Meloxicam after heating