COMPARISON BETWEEN DIFFERENT COMERICAL BRANDS OF MELOXICAM AND THEIR DEGRADATIONS AVAILABLE IN ZAWIA PHARMACIES, LIBYA

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Abstract

Meloxicam is an enolic acid derivative, which is the most important of the non-steroidal anti-inflammatory drug (NSAID). The objective of this work was to measure the absorbance of commercial meloxicam brands and their percentage of degradations under different conditions, as defined under the International Conference on Harmonization (ICH) guideline by using a spectrophotometer. The degradation behaviour of meloxicam was studied by subjecting the different brands of meloxicam to hydrolytic (acidic and basic), photolytic (Ultraviolet) and thermal stress. The collected data helped to identify the degradation products of the drug. The results showed a different pattern of degradation in all cases.

Keywords: Meloxicam; commercial; degradation; ultraviolet; spectrophotometer.

Introduction

Meloxicam is an NSAID, which falls under the oxicams class. It is given to reduce the symptoms of arthritis (juvenile rheumatoid arthritis, osteoarthritis, and rheumatoid arthritis), such as inflammation, swelling, stiffness, and joint pain (Xu *et al*,. 2014).

Chemically, the international union of pure and applied chemistry (IUPAC) name of meloxicam is 4-hydroxy-2methyl-N (5-methyl-2-thiazolyl) -2H-1,2-benzothiazine-3carboxamide-1,1-dioxide with the chemical formula ($C_{14}H_{13}N_3O_4S_2$), and its molecular weight is 351.4 g/mole Figure. (1).

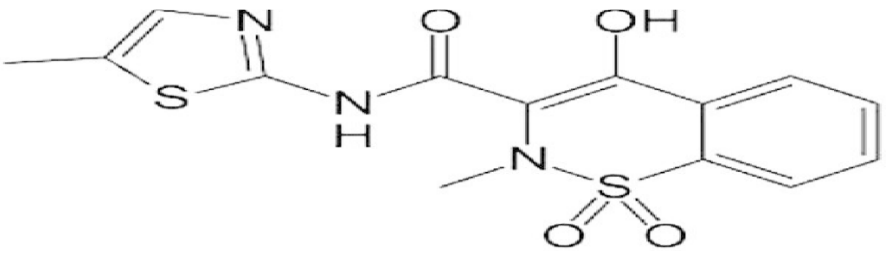

Figure (1): Shows the Chemical Structure of Meloxicam.

Nowadays, meloxicam is commercially available as tablets, capsules, disintegrating tablets, or oral suspensions; it can also be injected directly into the bloodstream by a healthcare professional. It is found in pharmacies under the brand names Mobic, Mobitil, Vivlodex, Qmiiz, and Anjeso, (Corveleyn and Remon, 1997).

Meloxicam is also effective at reducing inflammation, pain, and swelling if associated with arthritis. Its COX-2 inhibitor NSAIDs decreases the production of prostaglandins by blocking the cyclooxygenase (COX-2) enzyme. 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 (Arias *et al*,. 2018).

Meloxicam is classified as a BCS Class II drug (high permeability and low solubility), has a log p=3.42, and a poor wettability in water, causing difficulties in the pharmaceutical formulations design. Besides, the skin barrier properties limit the permeability of various pharmaceutical active substances, requiring appropriate drug delivery systems to produce optimal therapeutic effect (Bachhav and Patravale, 2010; Khurana *et al*,. 2013).

Like all medications, meloxicam can have side effects such as abdominal pain, diarrhoea, heartburnnausea, indigestion, and indigestion gas. Medication can also cause headache, dizziness, back pain, and flu-like symptoms among others (Ellsworth *et al*,. 2003).

In comparison with other NSAIDs, meloxicam is more potent than most NSAIDs. A once daily dose of 7.5–15 mg per oral is sufficient to elicit the desired effect in adults. In the case of ibuprofen for example, 400–600 mg three to four times a day is recommended. Its half-life of about 20 is also long and therefore it has a longer duration of action (da Silva and Woolf, 2010).

A variety of analytical methods, including UV spectrophotometry, have been developed and established to measure the concentration of meloxicam. Meloxicam can be quantitatively determined by using the direct or indirect spectrophotometric method to measure the absorption of monochromatic light in the near-ultraviolet region (200-400 nm). UV spectrophotometer can also be used for degradation studies (Garcia *et al*,. 2000; Nagwara *et al*,. 2005).

The method was validated and applied for the determination of meloxicam, including stress degradation in the different brands. It was validated in accordance with ICH guidelines (International Conference of Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use 2010) (Nemutlu and Kır, 2003; International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use, 2010).

UV degradation is the main problem in numerous UV-unstable products that 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; nonstop exposure is a major problem than intermittent exposure (Nageswara Rao *et al*,. 2010).

Acid/base forced degradation testing is used to evaluate the degradation of a drug substance by exposing its primary degradation products to basic or acidic medium overtime. Acid/base hydrolysis takes place in labile carbonyl functional groups e.g. Alcohols, imines, imides amides (lactams), esters (lactones), arylmines, and carbamates (Safila *et al*,. 2014).

Forced degradation is capable of demonstrating that stability-indicating technique is appropriate and can be used to identify degradation product rise and the subsequent loss of the active constituent (Safila *et al*,. 2014; , Safila *et al*,. 2014).

The aim of the study to measure the absorbance of different brands of meloxicam and their percentage of degradation under hydrolytic (acidic and basic), photolytic and thermal stress conditions. Moreover, this study provides information on the intrinsic stability of the drug molecule and helps in developing and validating stability-indicating analytical procedures.

Materials and Methods

Study location

The study was conducted in the Department of Medicinal Chemistry and Analytical chemistry laboratory, which is within the Faculty of Pharmacy, University of Zawia.

Materials

All the materials were of pharmaceutical grade. The laboratory reagents used were of an analytical grade and included methanol, ethanol, sodium hydroxide, and hydrochloric acid of 37% purity.

Apparatus

All spectral and absorbance measurements were performed by ‘PG’ UV-VIS spectrophotometer with matched 1 cm quartz cells. All the weights were weighed using analytical weighing balance (Pioneer OHAIUS Item PA214C, Italy) while pH measurements were taken using a digital pH meter (Jenway).Water Bath with ‘HH-4’ (DGT and CNST temperature tank) was used to heat and prepare the samples. All the glass materials were made of Pyrex glass; they were a stirrer, measuring cylinder, volumetric flask, pipette, and funnel. Glassware was initially washed with chromic acid then rinsed with distilled water and finally with deionized water which was freshly prepared.

Method of Analysis

Preparation of the standard graph of meloxicam

Ten milligrams of meloxicam powder (with a potency of 100.3%) were weighed in 100mL volumetric flask and dissolved with freshly prepared phosphate buffer solution of pH 7.4 to produce a 100 µg/mL standard stock solution. In order to fully dissolve meloxicam, the solution was sonicated for 30 min. Working standards of 4, 8, 10, 12, 16 and 20 µg/mL were prepared by transferring 2, 4, 5, 6, 8 and 10 mL of the stock solution into 50 mL volumetric flasks and diluting to the mark using the buffer solution. To obtain the wavelength of the maximum absorption, the 20µg/mL working standard was scanned in the UV spectrophotometer in the 240 –450 nm. The wavelength of the maximum absorption was noted. Absorbance values of the 6 working standard solutions at this wavelength were recorded and, from this data, the calibration curve of meloxicam was plotted.

Preparation of meloxicam solution of different brands

Three tablets of each brand were separately weighed using an analytical balance. The tablets were separately powdered with the help of mortar and pestle. 10 mg of each brand was weighed and transferred to a 100 mL Beaker. MOBIC, MOBITIL, MELOXICAM brands were dissolved in a small quantity of distilled water to prepare the primary solutions of meloxicam then they were mixed. The solution was filtered and the clear solution was diluted. The solutions were transferred into three 100ml volumetric flasks. The absorbance of each brand (20µg/mL) was determined by using a UV-Visible spectrophotometer at 400nm.

Procedure for degradation Studies

The degradation studies were performed by determining the effect of heat, UV, acid, and base on the solution of three brands of meloxicam. The effect of heat and UV light on MOBIC (M1), MOBITIL (M2), and MELOXICAM (M3) were determined by transferring 5 ml solution (100µg/mL) of each brand to the six different test tubes that contain the same solution of each brand.5 mL of distilled water was added to each of the six test tubes to obtain new concentrations of the solution of 100µg/mL.

Hydrolytic reactions were carried out in acidic and alkaline using hydro-chloric acid (0.1 N), sodium hydroxide (0.1 N) respectively. In each case, the temperature was maintained at room temperature for 30 minutes.

Photolytic studies were conducted in a photostability chamber and kept in Ultraviolet light for 30 min at 256 nm. For thermal stress studies, the brands were sealed in glass vials and placed in a thermostatic block at 50ºC for 60 min. UV-Visible spectrophotometer was used for determining the absorbance of each solution at a wavelength max of 400 nm.

Results and Discussion

The results are presented in the form of Tables (1) and (2) with some explanations.

Table (1): Absorbance of Different Brands of Meloxicam.

Parameters	Absorbance		
	MOBIC	MOBITIL	MELOXICAM
Before	2.073	2.190	0.656
Acid	1.5	1.497	1.493
Base	1.385	1.381	1.380
UV	1.641	0.343	0.879
Heat	0.558	0.563	0.315

Table (2): Percentage of Different Brands of Meloxicam.

Parameters	Percentage of degradation		
	MOBIC	MOBITIL	MELOXICAM
Acid	72.36	68.35	227.59
Base	66.81	63.05	210.36
UV	79.16	15.66	133.99
Heat	26.91	25.70	48.01

The most important findings of this study are discussed in this part. We have conducted a study on force degradation parameters of three different brands of meloxicam i.e. MOBIC, MOBITIL, MELOXICAM. Their absorbance for degradation parameters (acid, base, UV, and heat) before and after treatment is demonstrated in Table (1). The percentage of degradation of different brands of meloxicam is shown in Table (2) and their graphical representation is shown in Figure (2).

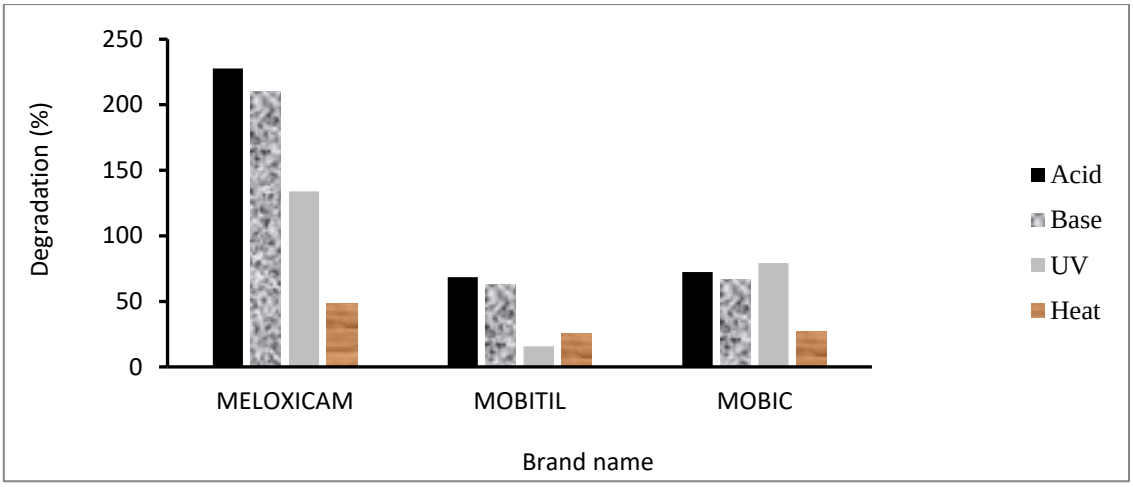

Figure (2): Degradation Pattern of Different Brands of Meloxicam.

When MOBIC brand (M1) of meloxicam was subjected to NaOH, HCL, U.V light, Heat (50^0C) significant changes in availability were observed of 66.81%, 72.35%, 79.16%, and 26.91% respectively. When MOBITIL brand (M2) was subjected to NaOH, HCL, U.V light, Heat (50^0C) significant changes in availability were observed of 63.05%, 68.35 % 15.66% and 25.70% respectively. On the other hand, MELOXICAM brand (M3) was also subjected to NaOH, HCL, U.V light, and heat (50^0C), significant changes in availability were also observed of 210.36%, 227.59%, 133.95% and 48.01% respectively.

Conclusion

Stress degradation studies, followed by UV spectrometry, yielded good information on the degradation behaviour of meloxicam under hydrolytic, photolytic and thermal stress conditions. According to USP, a meloxicam tablet contains not less than (NLT) 90.0 % and not more than (NMT) 110.0 % of the labelled amount of meloxicam. Solution of meloxicam is stable at room temperature, but demonstrated high susceptibility to degradation in alkaline and acidic environment. When chosen brands of meloxicam (M1, M2, and M3) were introduced in acid media, base media, UV light and heat, different significant degradation was observed in all brands. The UV spectroscopy analysis of the amount of degraded product is usually preferred over other methods because of less equipment cost and economical maintenance advantage.

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