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Effect of Acid and Base of Different Brands of Mefenamic Acid by UV Spectrophotometeric Method

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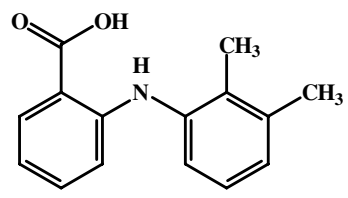
Mefenamic acid belongs to class of drug NSAIDS (non-steroidal anti-inflammatory drugs). Mefenamic acid inhibits the synthesis and actions of prostaglandins and it also block the COX-1 and COX-2 or COX enzyme. The purpose of this research is to study the effect of acid and base by using UV spectrophotometry, on different brands of mefenamic acid under ICH guideline Q1A (R2). According to USP, mefenamic acid contains not less than 98 % and not more than 102 % of $C_{15}H_{15}NO_2$ calculated on dried basis. The result concludes that when chosen brands of mefenamic acid *i.e.* dolor (A), postron forte (B), mefnac (C), positron (D), garden forte (E) were subjected to 0.1 N HCl (acidic medium), highly considerable degradation were observed in all the brands *i.e.* D (23.10 %), A (24.46 %), E (34.95 %), B (43.02 %) and C (66.34 %). Similarly when different brands of mefenamic acid were subjected to 0.1 N NaOH, highly considerable degradation were observed in the brand A, B (187.44 % and 124.38 %), C (51.93 %) and no degradation were observed in brand D and E (88.75 %) and (89.09 %). It is most commonly preferred as compare to other methods because of less time consuming and maintenance cost and can be use in routine quality control laboratories.

Keywords: Mefenamic acid, NSAIDS, Compounds, IUPAC formula.

INTRODUCTION

Mefenamic acid (MFA) belongs to class of drug NSAIDS (non-steroidal anti-inflammatory drugs) [1]. The IUPAC formula of mefenamic acid is 2-(2,3-dimethylphenyl)aminobenzoic acid [2] and molecular mass of mefenamic acid is 241.285 g/mol [3] and chemical formula of mefenamic acid is $C_{15}H_{15}NO_2$. The structure of mefenamic acid is [4].



Structure of mefenamic acid

It is odorless, microcrystalline powder [5]. Mefenamic acid inhibits the synthesis and actions of prostaglandins and it also block the COX-1 and COX-2 or COX enzyme [6]. Bioavailability of mefenamic acid is 90 %. It is 90 % protein binding and it is metabolized by CYP-450 enzyme. Mefenamic acid is excreted by urine and faces [7]. It's commonly used to reduce the pain, menstrual pain, dysmenorrhea, migraine [8]. Most common side effects of GI upset, headache, vomiting, nausea, itching and skin rash and it also cause ulcers, holes in the stomach or intestinal bleeding [9]. Mefenamic acid is contra indicated in pregnancy [10].

Photolysis is estimated to be a major loss process for many of these compounds in including the common non-steroidal anti-inflammatory drug mefenamic acid. Quenching experiments proposed a direct reaction of mefenamic acid with excited triplet-state dissolved organic matter as the photosensitization process. The determination of the model photosensitizer proposes that the photosensitization by perinaphthenonearises by triplet-energy transfer by redevelopment of the sensitizer [11]. Infrared method developed and it is used to the thermal conversion of mefenamic acid to polymorphic I to the polymorphic II. Rates of conversion for the crystal to crystal transition have been measured at different temperatures and subsequently used to calculate the activation energy for the process. HPLC estimation was carried out to estimate the potential loss of analyte due to sublimation when samples of mefenamic acid are maintained at raised temperatures in the DSC preceding to determining the exothermic event indicative of the polymorph I content of a sample [12].

The purpose of present research is to study the effect of acid and base by using UV spectrophotometry, on different brands of mefenamic acid under ICH guideline Q1A (R2) by spectrophotometric method, it is most commonly preferred as

compare to other methods because of less time consuming and maintenance cost.

EXPERIMENTAL

Pyrex glass is used for all the glass materials used in this research including stirrer, measuring cylinder, volumetric flask, pipette and funnel. At the start of the work all the glass wares were rinsed by chromic acid than washed with water and finally with freshly prepared double distilled water or deionized water. The analytical grade reagents used in the working were, 0.1 N sodium hydroxide, 0.1 N hydrochloric acid and deionized or double distilled water. The active use was quinapril in the form of tablet.

Shimadzu double beam 1601 UV visible spectrophotometer, 'PG Instrument', with a cuvette (quartz). Weighing Balance of Pioneer OHAIUS (Item PA214C). Water Bath with 'HH-4' (DGT and CNST temperature tank).

Preparation of 0.1 N sodium hydroxide and hydrochloric acid: Hydrochloric acid (HCl) (37 % purity and 12 N normality) of Analytical grade was used for the preparation of 0.1 N HCl. In volumetric flask (L), preparation was carried out by transferring small quantity of water, also transferring 8.36 mL of hydrochloric acid in a volumetric flask and makes up the final volume with deionized water. 0.1 N NaOH was prepared by weighing 4 g of sodium hydroxide and transferring it, in a liter volumetric flask. Firstly take small portion of water and dissolve in NaOH and then make up the volume with deionized water up to the final volume of the volumetric flask [13].

Preparation of mefenamic acid solution: Individually weigh each tablet of the brand of mefenamic acid *i.e.* dollar, postron forte, mefnac, positron, garden forte. Ground and triturate the tablets in mortar pestle and convert them into powder form. Accurately weighed triturated powder equivalent to 25.16 mg of mefenamic acid in a teared beaker and dissolve them in small quantity of deionized water for making primary solutions of mefenamic acid and shake. The dissolved solutions were transferred into 100 mL volumetric flasks and finally make-up the final volume with deionized water. For the determination of absorbance of solutions of mefenamic acid, use of UV spectrophotometry at wavelength λ_{max} of 288 nm is considered.

Procedure for effect of acid and base on mefanamic acid: The degradation studies were carried out by analyzing the effect of acid and base on solution of the different brands of mefenamic acid. The effect of acid and base were determined by transferring 5 mL of each solution (200 ppm) of dollar, postron forte, mefnac, positron, garden forte in the ten different test tubes then add 5 mL of 0.1 N HCl solution in first test tube and 5 mL of 0.1 N NaOH solution in other test tube. All the test tubes (12 test tubes) were left for 0.5 h. UV-visible spectrophotometer was used for determining the absorbance of each solution at wavelength λ_{max} of 215 nm [14].

Procedure for degradation studies: The degradation studies were carried out by analyzing the effect of acid and base on Shimadzu double beam 1601 UV visible spectrophotometer, solution of five different brands of mefenamic acid [dolor (A), postron forte (B), mefnac (C), positron (D), garden forte (E)] available in Karachi, Pakistan. Initially the effect of acid was determined by transferring 5 mL solution of each brands of mefenamic acid A, B, C, D and E (200 ppm) in 5 test tubes respectively. Similarly the effect of base was determined by transferring 5 mL solution of each brand of mefenamic acid A, B, C, D and E (200 ppm) in five test tubes correspondingly. Add 5 mL of hydrochloric acid solution (0.1 N) in first set of four test tube and 5 mL of sodium hydroxide solution (0.1 N) in second set of four test tubes respectively. Now all the test tubes (10 test tubes) were left for 0.5 h in their particular environment. With the help of UV-visible spectrophotometer, after 0.5 h, determine the absorbance of the each solution at wavelength λ_{max} 275 nm [15].

RESULTS AND DISCUSSION

We have conducted research on five different brands of mefenamic acid [dolor (A), postron forte (B), mefnac (C), positron (D), garden forte (E)] for analyzing the effect of acid and base. The absorbance of all the brands of mefenamic acid after acid and base is shown in Table-1. The percentage of degradation of different brands of mefenamic acid is shown in Table-2 and their degradation pattern in graphical form is shown in Fig. 1.

TABLE-1
ABSORBANCE OF DIFFERENT BRANDS OF MEFENAMIC ACID

Parameter	Absorbance				
	Mefnac	Dolor	Posnstan forte	Ponstan	Gardan forte
Before	1.21	1.985	2.02	1.182	3.044
Acid	0.296	0.854	1.34	0.273	1.064
Base	2.268	2.469	1.049	1.049	2.712

TABLE-1
DEGRADATION (%) OF DIFFERENT BRANDS OF MEFENAMIC ACID

Parameter	Degradation (%)				
	Mefnac	Dolor	Posnstan forte	Ponstan	Gardan forte
Acid	24.46	43.02	66.34	23.10	34.95
Base	187.44	124.38	51.93	88.75	89.09

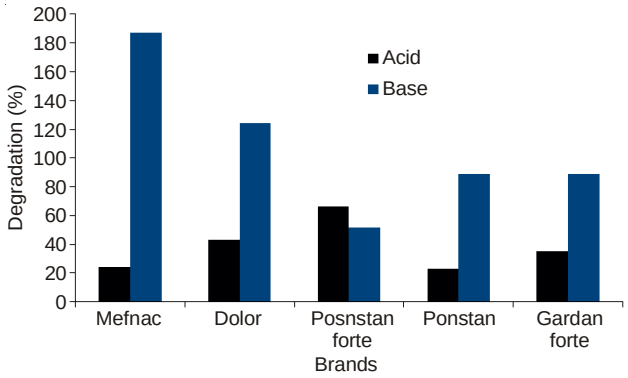


Fig. 1. Degradation pattern of different brand of mefenamic acid

When the five brands of mefenamic acid; dolor (A), postron forte (B), mefnac (C), positron (D), garden forte (E) were subjected to 0.1 N HCl, highly considerable changes in

availability were observed in D (23.10 %), A (24.46 %), E (34.95 %), B (43.02 %) and C (66.34 %). Similarly when different brands of mefenamic acid were subjected to 0.1 N NaOH, highly considerable changes were observed in A, B (187.44 % and 124.38 %), C (51.93 %) and slight changes were observed in brand D and E (88.75 %) and (89.09 %).

Conclusion

According to USP, mefenamic acid contains not less than 98 % and not more than 102 % of $C_{15}H_{15}NO_2$ calculated on dried basis. The result of the research work concludes that when chosen brands of mefenamic acid *i.e*. dolor (A), postron forte (B), mefnac (C), positron (D), garden forte (E) were subjected to 0.1 N HCl (acidic medium), highly considerable degradation in all the brands (A, B, C, D and E) and when all the chosen brands were subjected to 0.1 N NaOH, highly considerable degradation were observed in A, B and C and no degradation was observed in brand D and E.

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