The National Ribat University
Faculty of Graduate studies and scientific research

Development of Spectrophotometric Method for Post Marketing Surveillance of Different Brands of Mefenamic Acid Tablets

A thesis submitted in partial fulfillment of the requirements of M.pharm in Drug Quality Control

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Dedication

To my caring and loving parents for their continuous moral support to see me successful in life

To my dear sisters for their unlimited encouragement and my brothers for their kind assistance
Acknowledgement

Praise is to Allah, lord of the worlds who gave me the power to do and complete this work. I thank Allah for helping me through my life and along my steps till this moment and from whom I need his support always and for forever.

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I will be grateful forever for their love.
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<td>UV</td>
<td>Ultra Violet</td>
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<tr>
<td>GC</td>
<td>Gas Chromatography</td>
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<td>GLC</td>
<td>Gas – Liquid Chromatography</td>
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<tr>
<td>HPLC</td>
<td>High Performance Liquid Chromatography</td>
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<tr>
<td>TLC</td>
<td>Thin Layer Chromatography</td>
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<tr>
<td>DMF</td>
<td>Dimethyl formamide</td>
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<td>EDTA</td>
<td>Ethylene diamine tetra acetic acid</td>
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<tr>
<td>ABS</td>
<td>Absorbance</td>
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<td>B.P</td>
<td>British Pharmacopoeia</td>
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<tr>
<td>U.S.P</td>
<td>United State Pharmacopoeia</td>
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<tr>
<td>B.NO</td>
<td>Batch Number</td>
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<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
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<td>NSAID</td>
<td>Non-Steroidal Anti-inflammatory drugs</td>
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<td>COX</td>
<td>Cyclooxygenase enzyme</td>
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<tr>
<td>Df</td>
<td>Degree of freedom</td>
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<tr>
<td>Ms</td>
<td>Mean square</td>
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4.1 Discussion

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Abstract

Background:

Post market surveillance of drugs is important to follow their stability under different climatic and storage conditions.

Mefenamic acid is one of the mostly used Non-Steroid-Antinflammatory drugs (NSAID). Therefore, physicochemical evaluation of Mefenamic Acid tablets is considered important to ensure its quality, safety and stability.

The aim of this study was to develop a simple, precise, efficient UV-Spectrophotometric method for the assay of different brands of Mefenamic Acid.

Statistical comparison of the results obtained using the developed UV-Spectrophotometric method with official B.P titration method.

Methods:

The collected brands of Mefenamic Acid tablets were assayed using the official B.P titration method. The titrant used was 0.1M Sodium Hydroxide using Phenol Red indicator. The developed UV- Spectrophotometric method utilize Methanol as solvent. The solution of standard Mefenamic Acid was scanned between 200 – 400 nm to find the lamda max(λ max) which can be used for the assay of the drug.

The selected wavelengths were found to be 348 and 280.5 nm. Beer’s law was applied to calculate the % content.

Results:

Results for the titration method for brand A was found to be 100.75% and for brand B to be 100.70% and for brand C was found to be 99.53%.

Results for the UV-spectrophotometer method for brand A was found to be 97.54% and for brand B to be 95.87% and for brand C was found to be 99.85%.

The statistical results obtain for the assay of the brands using the UV-Spectrophotometric method compared with the official B.P titration method reflected satisfactory the accuracy and precision of the developed UV-Spectrophotometric method according to the obtained t and F-value.

Conclusion:

The developed UV-Spectrophotometric method was successfully applied for assay for the three different brands. All the brands were found to fall within the accepted official limit indicating their good quality and safety.
الملخص

خلفية:

مراقبة سوق الأدوية بعد التسويق مهمة لمتابعة استقرارها تحت مختلف الظروف المناخية والتخزين. حمض الميفيناميك هو واحد من الأدوية الستيرويدية مضادة للالتهاب ومسكنه. لذا التقييم الفيزيائي لأقراص حمض الميفيناميك هو النظر في الأهمية لضمان جودتها والسلامة وعدم استقراريتها. وكان الهدف من هذه الدراسة هو استعمال طريقة بسيطة وفعالة (طريقة الأشعة فوق البنفسجية الطيفية) لتحليل أقراص حمض الميفيناميك من ماركات مختلفة.

المقارنة الإحصائية للنتائج التي تم الحصول عليها باستخدام طريقة الأشعة فوق البنفسجية مع طريقة الدستوري الرسمي.

الأساليب:

معيارية العلامات التجارية التي تم جمعها من أقراص حمض ميفيناميك باستخدام طريقة المعاملة الرسمية. وكان محلول المعامل المستخدم 0.1 مولاري هيدروكلوريد الصوديوم باستخدام مؤشر الفينول الأحمر. وطريقة الأشعة فوق البنفسجية المقدمة تستعمل الميثانول كذيب تم تفحص حمض ميفيناميك القباسي بين 200-400 نانومتر للعثور على ماكس \( \lambda \) والتي يمكن استخدامها لفحص الدواء. تم العثور على موجات اختيارية ليكون 348 و 280.5 نانومتر. تم تطبيق قانون بير حساب المحتوى المئوي.

النتائج:

تم العثور على نتائج لأساليب المعاملة الدستورية للعلامة التجارية أن يكون 100.75 % والعلامة التجارية ب أن يكون 100.70 %، والإدارة التجارية تم العثور على ج تكون 99.53 %.

تم العثور على نتائج لأساليب الأشعة فوق البنفسجية الطيفية للعلامة التجارية أن تكون 97.54 %.

والعلامة التجارية ب تكون 95.87 % والعلامة التجارية تم العثور على ج تكون 99.85 %.

B.P المعايرة الرسمية يمكن مدي دقة طريقة الأشعة فوق البنفسجية الطيفية التي وضعت وفقا لقيمته وقيمة F.

الإسناتج:

تم تطبيق طريقة الأشعة فوق البنفسجية الطيفية نجحت في تحليل ثلاثة علامات تجارية مختلفة.

تم العثور على جميع العلامات التجارية لتسقط مع الحد الرسمي القبول مبدأ نعية جيدة والسلامة.

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Chapter one
Introduction and literature
Review
1.1 Mefenamic Acid  background:

1.1.1 Definition:

Mefenamic Acid is a member of the anthranilic acid derivatives, Its name is derived from its systematic name (2-[(2,3-dimethylphenyl)amino] benzoic acid) Mwt = 241.285 g/mol. It is a Non-Steroidal Anti-inflammatory drug, analgesic and antipyretic properties. Mefenamic Acid is used to treat moderate pain and menstrual pain [1]. It is extensively used in the treatment of many diseases like rheumatoid arthritis, osteoarthritis, non-articular rheumatism and sport injuries. There is evidence that supports the use of Mefenamic Acid for pre-menstrual migraine headache prophylaxis, with treatment starting 2 days prior to the onset of flow or 1 day prior to the expected onset of the headache and continuing for the duration of menstruation [2].

![Mefenamic Acid structure](image)

Figure: 1 Mefenamic Acid structure

1.1.2 Chemistry:

Mefenamic Acid is a white to off-white, microcrystalline powder [3]. Practically insoluble in water, slightly soluble in alcohol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides, Melting point: 230-231°C, It shows polymorphism [4]. Water solubility 20mg/L (at 30 °C) [5].
1.1.3 Mechanism of action:

Like other members of the anthranilic acid derivatives (or fenamate) class of NSAID drugs, it inhibits both isoforms of COX and prevents formation of prostaglandins[6] [7].

1.1.4 Synthesis:

Analogous to fenamic acid, this compound may be synthesized from 2-chlorobenzoic acid and 2,3-dimethylaniline.[8]

1.1.5 Spectroscopy:

It has been reported that Mefenamic Acid M ethanloic solution exhibits absorption maxima at 280.5 nm (A1%1Cm = 415.6), and at 348 nm (A1%1C= 320).

1.1.6 Methods of Analysis:

Methods used in analysis are mainly Titrimetric methods (Aqueous or Non-aqueous Acid-Base titrations, Argentimetric, Complexometric, Oxidation-Reduction, Conductimetric Potentiometric), Spectrophotometric methods (UV-Visible, Flame Photometry), Chromatographic methods (GC, GLC, HPLC and TLC) and others. However, in this work we will focus on the mostly used analytical methods (Titimetry and Spectrophotometry) [13]

1.1.6.1 Titrimetric analysis:-

Titrimetric methods are still widely used in pharmaceutical analysis because of their robustness, cheapness and capability for high precision. The only drawback of this method that they lack is specificity [29]. This is based on chemical reactions rather than on physical properties. It involves a reaction between the substance to be measured (analyte) and a solution of a reagent known as titrant of a known concentration such as normality.

This reaction in general is represented as follows:

\[ aA + bB \rightarrow \text{Products} \]

\[ a, b = \text{Number of moles.} \]

\[ A, B = \text{Reactants.} \]

The point at which the amount of the titrant added equals chemically to the analyte is known as the equivalence point (theoretical end point or stoichiometric end point). The experimentally
obtained estimation of the equivalence point in the titration is referred to as end point. The two common ways of detecting the end point in acid-base titration are by the use of visual indicators or Hydronium ion indicating electrodes (glass and reference electrode). [13]

This method is referred to as Potentiometric titration, mostly useful for the titration of weak acids or bases to give more accurate end point detection. A precise and accurate quantitative titrimetric analysis is governed by the type of reaction which should be quantitative (not less than 99.9%), rapid with type of reaction time and occur in a single well-defined process to allow the accurate calculation of the analyte content. In addition, an accurate method for determining the equivalence point should be available [13]. Titration methods can be divided into three types:-

1.1.6.1 Direct Titration:-

Straight forward titration of the titrant with the substance to be determined. Example assay of dimercaprol injection, which involves the oxidation of the thiol groups with iodine [13].

1.1.6.1.2 In-Direct Titration :-

Involves the addition of a reagent to the substance to be determined which releases an intermediate at an equivalent amount, followed by the titration of this intermediate with a suitable titrant. Titrations of a copper salt is a good example: potassium iodide is added to the copper salt forms cupric iodide (unstable) that releases equivalent amount of iodine which is titrated with sodium thiosulphate using starch as indicator [13].

1.1.6.1.3 Back Titration :-

Involves the addition of an excess standard volumetric solution (exact volume $V_0$) to the substance to be determined and the titration of the excess ($V_1$) and subtraction to get the volume of the reacted standard volumetric solution ($V_0 - V_1$). Calculation of the concentration of the substance is obtained by the use of following formula:-

$$
\frac{V_0 - V_1 \times F \times E \times 100}{\text{Weight of active ingredient taken or volume}}
$$

$V_0 = \text{Exact volume of titrant}$

$V_1 = \text{Excess volume of titrant}$

$F = \text{Factor of Sodium Hydroxide}$

$E = \text{Titre value of Sodium Hydroxide}$

Back titration with a blank determination is important when either the volumetric solution is unstable or the volumetric solution can change its strength (Normality or Molarity), during titration especially on heating.[13]
1.1.6.1.4 Acid –Base Titration in aqueous media:-

An acid-solution is a solution in which Hydrogen ion (H+) concentration is greater than $10^{-10}$.

The strength of the acidity depend upon the dissociation constant the degree of ionization of the acid and the subsequent release of an equivalent amount of Hydrogen ions or protons. An acid is therefore, a proton donor, pH = -$\log[H]$ . An alkali solution is a solution in which hydrogen ion H+ concentration is less than $10^{-7}$. The strength of alkalinity depends on the dissociation constant, the degree of ionization of the base and the subsequent release of an equivalent amount of {OH}. A base is therefore, a proton acceptor. The pH depends on the [OH] . Acid-Base titration forms the most simple, rapid and widely applied method. Aqueous titrants are sodium hydroxide (Na OH) for acids and hydrochloric acid (Hcl) for bases. End point detection is usually determined by visual indicators or by a pH meter with a glass indicator electrode and a suitable reference electrode [13].

1.1.6.1.4.1 Acid –Base indicators:-

These are usually organic dyes that are either weak acids or weak base with different colors for the acidic or the basic form (two-color indicators). Some others are one-color (one form is colored and the other form is colorless). Phenolphthalein is colorless in acid and is pink in alkaline media. Indicators change from acidic color to the basic color cover a range of two pH limits (pH = $pK_a\pm 1$).

1.1.6.1.5 Acid –base titration in Non-aqueous solvent:-

Non-aqueous titration is a simple method, offers great advantages such as speed and ease of preparation and procedures, relatively fast response, reasonable selectivity, wide linear dynamic range, and low cost.[30]

Water being a cheap and easily obtainable solvent is replaced by another solvent only when necessary; Practically, it is replaced when we have either too weakly acidic or too weakly basic substances that do not give sharp end points in aqueous media, and when the compounds are insoluble in water and soluble in organic solvents[13].

Non-aqueous titration involves the use of a material devoid of water and therefore the use of dry utensils (flask and pipettes) through the assay process. The principle of method depends on either the titration of weakly basic compounds, dissolved in glacial acetic acid, against Perchloric acid in glacial acetic acid or the titration of weakly acidic substance dissolved in a suitable solvent such as Dimethylformamide (DMF) against Tetrabutylammonium Hydroxide, lithium or Potassium Methoxide [13].
1.1.6.1.6 Complexometric titration :-

This involves the complex formation between a metal and aligned (aligned is an electron-pair donor ion or molecule). There are two types of ligands: A ligand that can donate one pair of electrons (simple ligand) and ligands that can donate more than one pair of electrons (chelating agents). The mostly used ligand is the chelating agent Ethylenediamine tetra acetic acid [EDTA] which forms complexes with cations in a 1:1 ratio irrespective of the valence of the cation. EDTA-metal complexes are normally stable at wide range of pH. Most metals can be titrated in pH range 9-10. End-point detection is similar to those of the other titration methods. [13]

1.1.6.1.7 Argentimetric titrations:-

It is also known as precipitation titrations as it is the quantitative precipitation of halides with silver nitrate which is common reagent for such titration. It is divided to two types :-

- direct titration (Mohr"s method) and Back titration (Volhard"s method)[13]

1.1.6.1.8 Oxidation - Reduction titrations:-

It involves the loss or gain of electrons, oxidation and reduction in a system occur at the same time. Common oxidizing agents used in the volumetric analysis include potassium permanganate, potassium iodate, potassium dichromate and ceric sulphate.[13]

1.1.7 Spectrophotometric method:-

Many types of spectrophotometers are commercially available. The spectral ranges of these instruments depend on the choice of the light source, optical materials, monochromator and detector. The instruments covering the UV-Visible regions include :-

- Light source: for UV-Visible Quartz and Tungsten lamp
- Range for UV-Visible: UV (190-350 nm) Visible (350-700 nm)
- Wave length selector: Monochrometer or filter.
- Absorption cell: Quartz cell for UV and glass or plastic cell for visible
- Detector which is composed from: photocell, amplifier, read-out or recorder.

Spectrophotometers are: single beam, double beam, dual wave length and derivative spectroscopy. In the single beam spectrophotometers, there is only one light beam passing from the light source to the absorption cell to the detector, while in the double beam spectrophotometers, the light from the source passes through a monochromator which splits the
light into equal separate beams one passing through the sample and the other is for reference or blank.[13].

The assay of an absorbing substance may be quickly carried out by preparing a solution in a transparent solvent and measuring its absorbance at a suitable wavelength. The wavelength normally selected is a wavelength of maximum absorption (\( \lambda_{\text{max}} \)) where small errors in setting the wavelength scale have little effect on the measured absorbance. Ideally, the concentration should be adjusted to give an absorbance of approximately 0.9 around which the accuracy and precision of the measurement are optimal. The preferred method is to read absorbance from the instrument display under non-scanning conditions, i.e., with the monochromator set at analytical wavelength. Alternatively, the absorbance maybe read from a recording of the spectrum obtained by using a recording double-beam spectrophotometer. The latter procedure is particularly useful for qualitative purpose and in certain assays in which absorbances at more than one wavelength are required. The concentration of absorbing substance is then calculated from the measured absorbance.[14]

Quantitative analysis by UV-Visible absorption spectrometry is practiced by almost every analytical laboratory. Most organic, inorganic and biochemical substances can be determined either directly or after the formation of an absorbing derivative or complex.[15]

In spectrophotometric analysis a source of radiation is used that extends into the UV-Visible regions of the spectrum. Absorption of radiation in these regions of the electromagnetic spectrum results in electronic transitions between molecular orbital. This corresponds to a wavelength range of 200-800 nm. The amount of absorbing radiation is proportional to concentration of absorbing substance and this is ruled by Beer’s Law. All molecules can undergo electronic transitions, but in some cases absorption occurs below 200 nm, like saturated hydrocarbons, unsaturated groups, known as chromophore, are responsible for absorption mainly in the near UV and Visible regions and are of most value for quantitative analysis. The positions and intensities of the absorption bands are sensitive to substituent close to the chromophore, to conjugation with other chromophore and to solvent effects. Saturated groups containing hetero atoms which modify the absorption due to a chromophore are called auxochromes and include –OH, -CL,-OR and –NR2[15].

1.2 Literature review:

Mefenamic Acid was listed in British Pharmacopeia, 2003, volume3, which recommends aqueous titration method for its assay.

A potentiometric mefenamate ion sensor was developed for the determination of Mefenamic Acid in pharmaceuticals and in the human blood serum by using simple electrode Pt/Hg/Hg2(Mf)/ Graphite. This electrode responds to Mefenamic Acid with sensitivity of 58.9±0.7 mv.
Anon-aqueous was developed using Tetra-n-butylammonium Hydroxide as titrant and acetonitril as a solvent.

A simple UV-Spectrophotometric assay of Mefenamic Acid was developed for comparison of the three different brands of Mefenamic Acid using water as a solvent. The absorbance of sample prepared was measured at 288 nm against the solvent blank.[16]

A Spectrophotometric method was developed for determination of Mefenamic Acid using 1,4-dioxane as a solvent for extraction, the absorbance was measured at 353.2 nm.[17]

A UV-Spectrophotometric method was developed for estimation of Mefenamic Acid in bulk and pharmaceuticals using 0.1N HCL as a solvent. $\lambda_{max}$ for Mefenamic acid were found to be 285 nm. Beer’s law was obeyed in the concentration range of 5-60 mcg mL$^{-1}$ with 10.2799x104 Lmol-1 cm1 [18].

A Simultaneous spectrophotometric determination of Mefenamic Acid in pharmaceutical preparations was developed. Using 0.01 M Methanolic Hydrochloric acid as solvent, the absorbance of the mixture was measured at 248, 279 and 351 nm.[19]

Spectrophotometric estimation of Mefenamic Acid from a binary mixture by dual wavelength and simultaneous equation methods.[20]

Spectrophotometric determination of Mefenamic Acid in pharmaceutical preparations via Arsenazo 3-Cerium3 reaction was proposed, it based on oxidation–reduction reduction between Mefenamic Acid and cerium(iv) ion, and subsequent Ce (iii) reaction with arsenazo(iii) reagent in acidic medium to produce greenish–blue complex and have absorption at 654 nm with molar absorptivity of $10731 \times 10^5$ l.mol$^{-1}$ cm$^{-1}$. [21]

A First Derivative Spectrophotometry was developed using Methanolic Hydrochloric acid solution as solvent for extracting the drugs from the formulations and subsequently the samples were evaluated directly by derivative spectrophotometry, Simultaneous determination of drug can be carried out using the zero-crossing and the graphical methods. The calibration graphs were linear in the ranges from $1.8 \times 10^{-6}$ to $1.6 \times 10^{-4}$ M of Mefenamic Acid.[22]

Colorimetric Determination of Two Nonsteroidal Anti-inflammatory Drugs Using P-Dimethylaminocinnamaldehyde was developed. It was based on the inter-action of the secondary aromatic amine with p-dimethyl-aminocinnamaldehyde in acidified absolute methanol medium to form very stable red $[\lambda_{max}$ at 538 nm in case of diclofenac sodium] or blue $[\lambda_{max}$ at 665 nm in case of Mefenamic Acid products]. Beer's law was obeyed over the ranges 10–80 $\mu$g ml$^{-1}$ and 1–8 $\mu$g ml$^{-1}$ for diclofenac sodium and Mefenamic Acid [23]

Novel Colorimetric assay of Mefenamic Acid was developed and based on a diazo coupling reaction using diazotized 4-amino-3,5-dinitrobenzoic acid as chromogenic derivatizing reagent[24].
A Spectrophotometric determination of anti inflammatory agents using N-bromosuccinimide was developed. Flufenamic and Mefenamic Acids react quantitatively with N-bromosuccinimide in an acidic medium whereas allopurinol and indomethacin can be determined with reproducible results in an aqueous pyridine solution. [25].

Spectrophotometric determination of Mefenamic Acid in pharmaceutical preparations was developed. The method is based on the charge-transfer complexation between Mefenamic acid as an n-electron donor and chloranil as a π-acceptor to form a violet chromogen measured at 540 nm and concentration of the studied drug in the range of 10–60 μg/mL.[26].

A High Performance Liquid Chromatographic Estimation of Drotaverine Hydrochloride and Mefenamic Acid in Human Plasma was developed. Reverse phase HPLC method for the quantitation of drotaverine hydrochloride and Mefenamic Acid in human plasma. Organic solvent system used for liquid extraction composed of dichloromethane, and isopropyl alcohol in the ratio 80:20 (v/v). The compounds were separated on a Thermo BDS Hypersil C8 (25.0 cm±1.4 mm,5 m particle size) column in isocratic mode with a mixture of acetonitrile and ammonium acetate buffer (20 mM, pH 3.5 ±0.05 adjusted with 85% phosphoric acid) in a ratio of 55: 45 (v/v), as the mobile phase, at a flow rate of 1.0 mL min-1. The effluent was monitored by UV detection at 230 nm. [27]

Physical and chemical characterization of Mefenamic Acid in different pharmaceutical dosage forms and their stability studies were developed using novel RP-HPLC method, stability studies were developed. The method developed constitutes mobile phase ,acetonitrile:acetic acid : water(72.5:1:26.5,v/v/v) at pH 3 and Mefenamic Acid was monitored with UV-detection at 279 nm ,eluting out at 3.98 min. The present HPLC method was found to be linear (100-300 μg ml-1). The limit of detection was found to be 10μg ml-1[28].
1.3- Objectives:-

1.3.1 General objective:
Post market surveillance of the three brands of Mefenamic Acid tablet(500 mg) using official B.P titration method and developed UV-spectrophotometric for analysis.

1.3.2 Specific objectives:
- To develop simple, quantitative UV-spectrophotometric method for analysis of Mefenamic acid tablets( 500mg).
- Statistical evaluation of the results obtained by developed UV-spectrophotometric with the official B.P titration method.
- To evaluate the percent content of active pharmaceutical ingredient after release to the market (post market surveillance).
- Comparison of the results obtained for each brand with each other.
Chapter Two

Materials and Methods
2. Materials and Methods:

2.1 Materials, Reagents and Instruments:

2.1.1 Materials:

The materials used and their sources were summarized in the table (1)

Table (1): Materials

<table>
<thead>
<tr>
<th>Material</th>
<th>Company</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Mefenamic Acid working standard</td>
<td>Central lab</td>
<td>Khartoum - Sudan</td>
</tr>
<tr>
<td>Lot No-130915</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assay: 99.92%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss on drying: 0.36%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brand A</td>
<td>Bal Pharma limited</td>
<td>Mumbai - India</td>
</tr>
<tr>
<td>B.No mff 283</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFD: 6/2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EXP: 6/2018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brand B</td>
<td>Hikma pharmaceuticals</td>
<td>Amman - Jordan</td>
</tr>
<tr>
<td>B.No 0083</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFD : 1/2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EXP : 1/2018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brand C</td>
<td>General medicines company</td>
<td>Khartoum - Sudan</td>
</tr>
<tr>
<td>B.No L200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFD: 3/2016</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EXP : 3/2018</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.1.2 Reagents:

Reagents used are listed in table (2)

Table (2) Reagents used:

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Company</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute ethanol</td>
<td>Scharlau</td>
<td>Spain</td>
</tr>
<tr>
<td>Methanol</td>
<td>Cairo Erba reagents</td>
<td>S.A.S</td>
</tr>
<tr>
<td>Phenonaphthaline</td>
<td>BDH</td>
<td>England</td>
</tr>
<tr>
<td>Phenol red</td>
<td>Merck limited</td>
<td>Mumbai- India</td>
</tr>
<tr>
<td>Sodium Hydroxide</td>
<td>Scharlau</td>
<td>Spain</td>
</tr>
<tr>
<td>Potassium Hydrogen Phthalate</td>
<td>Merck limited</td>
<td>Mumbai- India</td>
</tr>
</tbody>
</table>
2.1.3 **Instruments and Apparatus:**

Instruments and Apparatus used are listed in table (3)

Table (3): Instruments and Apparatus used

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Company</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV-min-1240 spectrophotometer</td>
<td>Shimadzu</td>
<td>Japan</td>
</tr>
<tr>
<td>Electronic balance</td>
<td>Shimadzu</td>
<td>Japan</td>
</tr>
<tr>
<td>Bandelin sonorex</td>
<td>Bandelin Electronic</td>
<td>Germany</td>
</tr>
<tr>
<td></td>
<td>heinichstrasse 3-4 D-12207</td>
<td></td>
</tr>
<tr>
<td>Friabilatortrommel</td>
<td>Erweka GbhD-63150 heusenstamm</td>
<td>Germany</td>
</tr>
<tr>
<td>Disintegration device</td>
<td>(ZT 321 Germany)</td>
<td>Germany</td>
</tr>
<tr>
<td>Waterbath</td>
<td>Gesellschaft Fur Labor</td>
<td>Germany</td>
</tr>
<tr>
<td></td>
<td>techink 1032</td>
<td></td>
</tr>
<tr>
<td>Burette, conical flask</td>
<td>Iso Lab</td>
<td>Germany</td>
</tr>
<tr>
<td>Measuring cylinder,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volumetric pipette, Dropper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>,Beaker, Separating funnel,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnetic stirrer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter Paper</td>
<td>Bright</td>
<td>China</td>
</tr>
</tbody>
</table>
2.1.4 Standard and Samples Stock solutions preparation:

2.1.4.1 Preparation of Mefenamic Acid stock standard solutions for direct UV-spectroscopy:

A weight of 0.02g of Mefenamic Acid standard powder was dissolved in small amount of methanol and transferred to a 25ml volumetric flask. Then the volume was completed to the mark with methanol. From this solution 2ml was pipetted and transferred to 100 ml volumetric flask, the volume was completed to obtain solution containing 0.0016 w/v.

2.1.4.2 Preparation of Mefenamic Acid Sample solutions for direct UV-spectroscopy:

Three samples were taken from 20 tablets of Mefenamic Acid after being weighted and powdered. Weight containing 0.02g was taken and transferred to 25ml volumetric flask, about 15 ml methanol was added and shacked well for 15 mint by sonicator, then the volume completed to the mark with methanol (solution A). From this solution 2ml was pipetted and transferred to 100 ml volumetric flask and the volume was completed to the mark with methanol to obtain solution containing 0.0016 w/v.

2.1.4.3 Preparation of Mefenamic Acid Sample solutions for aqueous titration:

20 tablets were weighted and powdered, weight equivalent to 0.5 g of Mefenamic Acid powder was taken and transferred to 100 ml conical flask and about 80 ml of warm absolute ethanol previously neutralized to phenol red solution was added and altering between heating and ultrasound to aid dissolution then cooled, and sufficient amount of the neutralized absolute ethanol was added to complete volume.
2.2. Methods:

2.2.1. Physical tests:

2.2.1.1. Friability test:

10 tablets were being weighted and rotated in a friabilator at 25 rpm for 4 minutes. Then the tablets were de-dusted and weighted, and the loss of weight due to fracture or abrasion was recorded as % age weight loss (% friability), the method was repeated three times.

2.2.1.2 Weight Variation test:

10 tablets were taken, then each tablet was weighted individually using sensitive electronic balance and average weight was calculated. The results were compared with B. P. specification of weight variation test.

2.2.1.3 Disintegration test:

6 tablets were taken and kept in basket assembly suspended in a beaker containing distilled water maintaining at 37±0.5°C with up and down frequency of 27 to 33 cycles per minute. The time at which the tablets were completely disintegrated was taken and compared with the U.S.P specification. The method was repeated three times.

2.2.1.3 Hardness test:

Hardness test was done manually, number of tablets was taken from each brand and was broken by hand without being disintegrated.
2.2.2. Assay of the three Mefenamic Acid samples solutions using UV-Visible spectroscopy method:

Each sample solution was prepared at concentration (0.0016 g/100 ml) as mentioned in section (2.1.4.2). The absorbance of each was measured at the selected $\lambda_{\text{max}}$ 348 and 280.5 nm against blank containing methanol. The procedure was repeated three times and an average of the % content values was obtained.

2.2.3. Assay of the three Mefenamic Acid sample solutions by aqueous titration:

A weight of 0.5 g was accurately weighed and prepared as mentioned in section (2.1.4.3), Then titrated with 0.1M NaOH VS using phenol red as indicator. Each ml of 0.1M NaOH VS was equivalent to 0.02413g of C15H15NO2. The method was repeated three times.
Chapter Three
Results
The three Mefenamic Acid samples solutions were assessed using simple UV-Visible spectroscopy methanol, then the method was compared with an official B.P titration method.

3.1 Results of Physical tests of the three brands of Mefenamic Acid tablets (500mg) are shown in table (4):

Table 4: Data of the physical tests carried for the three brands of Mefenamic Acid tablets (500mg):

<table>
<thead>
<tr>
<th>No</th>
<th>Brand's Name</th>
<th>Batch No</th>
<th>Friability%</th>
<th>Uniformity of weight(mg)</th>
<th>Disintegration time(min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Brand A</td>
<td>Mff283</td>
<td>0.241</td>
<td>0.7840 ± 0.015</td>
<td>2.15</td>
</tr>
<tr>
<td>2</td>
<td>Brand B</td>
<td>0083</td>
<td>0.025</td>
<td>0.7848 ± 0.005</td>
<td>8.30</td>
</tr>
<tr>
<td>3</td>
<td>Brand C</td>
<td>L200</td>
<td>0.350</td>
<td>0.7032 ± 0.0074</td>
<td>3.03</td>
</tr>
</tbody>
</table>

3.2 Chemical assessment results:

3.2.1 UV-Visible Spectroscopy Method:

3.2.1.1 Calculation of A%1cm of Mefenamic Acid standard solutions:

The three standard Mefenamic Acid solutions gave two absorbance values at $\lambda_{max}$ 280.5nm and 348nm. The absorbance value at $\lambda_{max}$280.5nm was obtained by procedure mentioned in section (2.2.2), then the mean absorbance value of the three replicates were calculated to find A%1cm using Beer's law.

$$A = A\%1cm \times b \times C$$

Where A is absorbance of Mefenamic Acid standard solutions, A%1cm = Beer's law constant (absorbtivity), b = Path length of cell and C is the concentration of standard solution. As each standard solution was prepared at concentration (0.0016 w / v).
Calculation of A1% 1cm of Mefenamic Acid standard solutions at 348nm:

\[ A_{1\%1\text{cm}} = \frac{A}{c} \]

\[ A_{1\%1\text{cm}} = \frac{0.512}{0.0016} = 320 \]

Calculation of A1% 1cm of Mefenamic Acid standard solutions at 280.5 nm:

\[ A_{1\%1\text{cm}} = \frac{A}{c} \]

\[ A_{1\%1\text{cm}} = \frac{0.665}{0.0016} = 415.62 \]

Figure (2): Absorption spectra of a 0.0016 w/v Mefenamic Acid standard solution.

3.2.1.2 Calculation of the % content for the three brands of Mefenamic Acid sample solutions by UV-spectroscopy:

The equation that used for calculation of sample % content by UV-spectroscopy is

\[ \left( \frac{\text{Actual concentration}}{\text{Theoretical concentration}} \right) \times 100\% \pm \text{SD} \]

The equation that can be used for calculation actual concentration of sample is
$A = A_1 \% \text{ cm} \times b \times C$

Where $A$ is absorbance of Mefenamic Acid sample solutions, $b$ is the path length of cell and $C$ is the concentration of sample solutions. As each sample solution was prepared at concentration (0.0016 w/ v). Table (5) shows the data obtained for the % content.

Example for calculation of the % content for brand A:

Weight of the 10 tablets = 7.9642 g.

Weight of the one tablet = 0.79642 g.

Weight equivalent to 0.02g active ingredient or weight to be taken = 0.0385 g.

Weight taken:

\[ W t_1 = 0.0318 \text{ g}, \quad W t_2 = 0.03189 \text{ g}, \quad W t_3 = 0.0318 \]

Corrected weight:

\[ W t_1 = 0.01996 \text{ g}, \quad W t_2 = 0.02 \text{ g}, \quad W t_3 = 0.02 \text{ g} \]

Absorbance:

\[ A_{b1} = 0.650, \quad A_{b2} = 0.656, \quad A_{b3} = 0.640 \]

Calculation of the concentration:

\[ A = A_1 \% \text{ cm} \times b \times C \]

\[ \therefore C = A / A_1 \% \text{ cm} \]

\[ C_1 = 0.650 / 415.6 = 0.00156 \text{ g/ ml} \]

\[ C_2 = 0.656 / 415.6 = 0.00158 \text{ g/ ml} \]

\[ C_3 = 0.640 / 415.6 = 0.00154 \text{ g/ ml} \]

% content = ( Actual concentration / Theoretical concentration ) \times 100

% content 1 = (0.00156 / 0.0016) \times 100 = 97.50 \%

% content 2 = (0.00158 / 0.0016) \times 100 = 98.75 \%

% content 3 = (0.00154 / 0.0016) \times 100 = 96.25 \%

Average % contents = 97.50 \%
Table (5): % Contents of the three brands of Mefenamic Acid by the UV-spectrophotometric method.

<table>
<thead>
<tr>
<th>Brand</th>
<th>Powder Wt taken in gram</th>
<th>Equivalent weight of active ingredient in g</th>
<th>Absorbance at 280.5nm</th>
<th>% content at 280.5nm</th>
<th>Average % content at 280.5</th>
<th>Absorbance at 348nm</th>
<th>% content at 348nm</th>
<th>Average % at 348</th>
</tr>
</thead>
</table>
| A     | 0.0318                  | 0.0199                                      | 0.650                  | 97.50               | 97.50±1.2
|       | 0.0319                  | 0.020                                       | 0.656                  | 98.75               | 98.80±1.2
|       | 0.0318                  | 0.0199                                      | 0.640                  | 96.25               | 96.25±1.2
| B     | 0.0314                  | 0.020                                       | 0.643                  | 96.69               | 95.87±0.9
|       | 0.0312                  | 0.0199                                      | 0.639                  | 96.01               | 96.01±0.9
|       | 0.0313                  | 0.020                                       | 0.631                  | 94.84               | 96.84±0.9
| C     | 0.0280                  | 0.020                                       | 0.655                  | 98.50               | 99.85±2.2
|       | 0.0283                  | 0.020                                       | 0.681                  | 102.41              | 100.00±2.4
|       | 0.0282                  | 0.020                                       | 0.656                  | 98.65               | 99.37±0.7

3.2.2 Calculation of the % content of the three brands of Mefenamic Acid sample solutions by titimetric method:

The equation used for calculation of the % content for the three brands of Mefenamic Acid sample is:

\[
\text{% content} = \left( \frac{E \times F \times V}{\text{weight or volume of sample taken}} \right) \times 100
\]

\[V_0 = \text{Exact volume of titrant}\]

\[V_1 = \text{Excess volume of titrant}\]

\[F = \text{Factor of Sodium Hydroxide}\]

\[E = \text{Titre value of Sodium Hydroxide}\]

Table (6) shows the % contents of the three brands of Mefenamic Acid by titimetric method
Example for calculation for brand A:

Wt of 20 tabs = 15.842 g.

Wt of one tablet = 0.7921 g.

Wt equivalent to 0.5 g of active ingredient or weight to be taken = 0.7921 g.

Wt taken:

W1 = 0.7921 g, W2 = 0.7924 g, W3 = 0.7923 g.

* Corrected weight:

W1 = 0.5 g, W2 = 0.5 g, W3 = 0.5 g

Volume of 0.1 M NaOH:

V1 = 22.6 ml, V2 = 22.7 ml, V3 = 22.8 ml

Calculation of % content:

% content 1 = \( \frac{0.02413 \times 0.92 \times 22.6 \times 100}{0.5} \) = 100.34 %

% content 2 = \( \frac{0.02413 \times 0.92 \times 22.7 \times 100}{0.5} \) = 100.70 %

% content 3 = \( \frac{0.02413 \times 0.92 \times 22.8 \times 100}{0.5} \) = 101.23 %

Average % contents = 100.75 %

Table (6) : % Contents of the three brands of Mefenamic acid by titimetric method:

<table>
<thead>
<tr>
<th>Brand</th>
<th>Wt taken in gram</th>
<th>Weight of active ingredient</th>
<th>Volume of Na OH in ml</th>
<th>% content</th>
<th>Average % content</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.6338</td>
<td>0.40</td>
<td>18.4</td>
<td>102.11</td>
<td>101.17 ± 0.87</td>
</tr>
<tr>
<td></td>
<td>0.6337</td>
<td>0.40</td>
<td>18.2</td>
<td>101.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.6336</td>
<td>0.40</td>
<td>18.1</td>
<td>100.40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7922</td>
<td>0.50</td>
<td>22.6</td>
<td>100.34</td>
<td>100.75 ± 0.45</td>
</tr>
<tr>
<td></td>
<td>0.7924</td>
<td>0.50</td>
<td>22.7</td>
<td>100.70</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7923</td>
<td>0.50</td>
<td>22.8</td>
<td>101.23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.9502</td>
<td>0.60</td>
<td>27.1</td>
<td>100.43</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.9505</td>
<td>0.60</td>
<td>27.4</td>
<td>101.37</td>
<td>100.99 ± 0.50</td>
</tr>
<tr>
<td>-----</td>
<td>--------</td>
<td>-------</td>
<td>--------</td>
<td>--------</td>
<td>---------------</td>
</tr>
<tr>
<td></td>
<td>0.9503</td>
<td>0.60</td>
<td>27.3</td>
<td>101.17</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>0.6242</td>
<td>0.40</td>
<td>18.2</td>
<td>101.00</td>
<td>100.35 ± 0.71</td>
</tr>
<tr>
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<td>0.6242</td>
<td>0.40</td>
<td>18.1</td>
<td>100.45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.624</td>
<td>0.399</td>
<td>17.9</td>
<td>99.59</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7805</td>
<td>0.50</td>
<td>22.7</td>
<td>100.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7801</td>
<td>0.4998</td>
<td>22.5</td>
<td>100.09</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7805</td>
<td>0.50</td>
<td>22.8</td>
<td>101.23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.9361</td>
<td>0.599</td>
<td>27.1</td>
<td>100.43</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.9361</td>
<td>0.599</td>
<td>27.1</td>
<td>100.43</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.9363</td>
<td>0.60</td>
<td>27.4</td>
<td>101.37</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0.5625</td>
<td>0.399</td>
<td>17.8</td>
<td>99.03</td>
<td>99.58 ± 0.56</td>
</tr>
<tr>
<td></td>
<td>0.5627</td>
<td>0.399</td>
<td>18</td>
<td>100.14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5626</td>
<td>0.399</td>
<td>17.9</td>
<td>99.59</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7031</td>
<td>0.499</td>
<td>22.3</td>
<td>99.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7033</td>
<td>0.499</td>
<td>22.4</td>
<td>99.49</td>
<td>99.533 ± 0.37</td>
</tr>
<tr>
<td></td>
<td>0.7034</td>
<td>0.499</td>
<td>22.5</td>
<td>99.91</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.844</td>
<td>0.599</td>
<td>26.8</td>
<td>99.32</td>
<td>99.63 ± 0.29</td>
</tr>
<tr>
<td></td>
<td>0.8441</td>
<td>0.599</td>
<td>26.9</td>
<td>99.69</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.8443</td>
<td>0.60</td>
<td>27</td>
<td>99.89</td>
<td></td>
</tr>
</tbody>
</table>
3.2.2 Comparison between the results obtained by the titration method and the UV- spectroscopy method for the three brands of Mefenamic Acid:

3.2.2.1 Statistical data :-

Table (7): Statistical data of the titration method and the UV- spectroscopy method for the three brands.

<table>
<thead>
<tr>
<th>Brand name</th>
<th>UV-spectroscopy method</th>
<th>Titration method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>SD</td>
</tr>
<tr>
<td>A</td>
<td>3</td>
<td>1.22</td>
</tr>
<tr>
<td>B</td>
<td>3</td>
<td>0.945</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>2.22</td>
</tr>
</tbody>
</table>

3.2.2.2 ANOVA :

Table (8): ANOVA for the comparison between the three brands of Mefenamic Acid by UV-spectroscopic method:

ANOVA

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>SS</th>
<th>df</th>
<th>MS</th>
<th>F</th>
<th>P-value</th>
<th>F crit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between Groups</td>
<td>23.93855</td>
<td>2</td>
<td>11.96928</td>
<td>4.930218</td>
<td>0.054139</td>
<td>5.143253</td>
</tr>
<tr>
<td>Within Groups</td>
<td>14.56642</td>
<td>6</td>
<td>2.427737</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>38.50497</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table (9): ANOVA for the comparison between the three brands of Mefenamic Acid by titration method:

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>SS</th>
<th>df</th>
<th>MS</th>
<th>F</th>
<th>P-value</th>
<th>F crit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between Groups</td>
<td>2.860867</td>
<td>2</td>
<td>1.430433</td>
<td>6.52603</td>
<td>0.031234</td>
<td>5.143253</td>
</tr>
<tr>
<td>Within Groups</td>
<td>1.315133</td>
<td>6</td>
<td>0.219189</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>4.176</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.2.2.3 t- and P-value for comparison between the UV-spectroscopy and the titration methods of three brands of Mefenamic Acid tablet (500 mg)

Table (10): t and F-value for the UV-spectroscopy method and the titration methods:

<table>
<thead>
<tr>
<th>Brand name</th>
<th>t-calculated</th>
<th>Degree of freedom</th>
<th>t-tabulated (p=0.05)</th>
<th>F-calculated</th>
<th>F-tabulated (p=0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>-4.29</td>
<td>2</td>
<td>3.182</td>
<td>7.399</td>
<td>19</td>
</tr>
<tr>
<td>B</td>
<td>-7.56</td>
<td>2</td>
<td>3.182</td>
<td>2.705</td>
<td>19</td>
</tr>
<tr>
<td>C</td>
<td>0.25</td>
<td>2</td>
<td>4.302</td>
<td>38.514</td>
<td>19</td>
</tr>
</tbody>
</table>
Chapter four
Discussion
4.1 Discussion:

One of the challenges for the pharmaceutical analyst is the possible circulation of counterfeit or substandard drugs or deteriorated drugs due to a number of factors.

Therefore, there is need for periodical assessment of drugs after marketing (post marketing surveillance).

Post marketing surveillance is always of utmost importance specially for the drugs of high frequency use (drugs for chronic diseases, analgesic,..ect).

On the other hand availability of simple, accurate, cost effective method for such assessment are needed.

Drugs circulating in Sudan are subjected to adverse climatic conditions beside the weak drug supply system which can lead to the deterioration of drug quality, loss of activity on formation of harmful degradation products. In this study we cared to evaluate the % content of the three brands of Mefenamic Acid to confirm their actual safety and efficacy. The chemical methods used in this study included direct spectrophotometric method (UV-Visible) and an official B.P titration methods.

Post market surveillance of some Mefenamic Acid samples available in Sudanese market gives a good overview about their stability during storage conditions and distribution.

It has been reported that Mefenamic Acid exhibits absorption maxima at 285 nm, It was deemed useful to make use of this reported method for assay of Mefenamic Acid using direct UV- spectrophotometric method. Absorption spectra were recorded over range 200-400nm to find the lamda max. The concentrations used were calculated to fall within limit of assay stated in the B.P (2003) (95 -105 %).The drug was found to have two lamda max at 280.5 and at 348. Both wave length were used for the assay of the drug according to Beer’s law.

The assay results for the three brands at the above mentioned wavelength were found as follows: At wave length 280.5 nm results for brand A [97.50 ± 1.22(n = 3)], brand B[95.87 ± 0.95(n =3)], brand C [ 99.85 ± 2.22 (n = 3) ] Table (5).
At 348 nm for brand A [97.08± 0.36 (n = 3)] , brand B [96.67± 0.37 (n =3)] ,
brand C [99.72± 0.32 (n = 3)]. Table (5)

All the results were found to be within specified limits B.P .2003 (95 -105 %).

Results for the official B.P titration method were found as follows :

Average of % contents for the three different weights taken for brand A [100 ± 0.58 (n = 9)],
brand B [100.59 ± 0.57 (n = 9)] , brand C [ 99.58 ±0.36 (n = 9 )] table (6). All the results were
found to be within specified limits B.P.2003 (95-105%).

The calculated t and F- values of the assay indicated that the developed UV-Spectrophotometric
was as accurate and precise as the official B.P titration method.

The precision of methods were evaluated by statistical analysis of data regarding standard
deviation of the three brands. Most SD values obtained for the UV-Spectrophotometric and
official titration method lie between the accepted SD values for assay ( less than 2% ) .

Generally, all the results were found within accepted limit of SD except for brand C(2.22) , the
difference could be due to possible interference with tablet excipients in the UV-
spectrophotometric method rather than in the titration method. Table (11)

Table (11): Summary of the results of assay for the three Mefenamic Acid samples:

<table>
<thead>
<tr>
<th>Brand name</th>
<th>UV- assay results</th>
<th>Titration assay results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 280.5 nm</td>
<td>At 348</td>
</tr>
<tr>
<td>A</td>
<td>97.50 ± 1.22(n=3)</td>
<td>97.08± 0.36(n=3)</td>
</tr>
<tr>
<td>B</td>
<td>95.87 ± 0.95(n=3)</td>
<td>96.67± 0.37(n=3)</td>
</tr>
<tr>
<td>C</td>
<td>99.85 ± 2.22(n=3)</td>
<td>99.72± 0.32(n=3)</td>
</tr>
</tbody>
</table>
The test hypothesis i-e ANOVA of assay of the three brands of Mefenamic Acid tablets by UV-spectroscopy showed no significant difference between the brands with this method, and ANOVA of assay of the three brands of Mefenamic Acid tablets by official B.P titration method showed no significant difference of all brands with this method.

The results for the physical tests were done as follows:

Disintegration test:

For analgesic drug rapid disintegration is preferred to attain rapid therapeutic effect. Disintegration results of brand A disintegrated most rapidly (2.15 minutes), brand B disintegrated at the slowest rate (8.30 mint) and brand C disintegrated at (3.03 minutes).

All these results lie with suitable disintegration test (maximum time 15mint) table (4).

Friability test:

In friability test all results were found to be within acceptable limit (not more than 1%) and suitable for transportation and handling without being broken. Table (4)

Weight variation test:

All tablets for weight variation were found to comply with the British Pharmacopoeia requirements (± 5%). Table (4)

Hardness test:

Hardness test was done manually. It was found to be acceptable which confirm friability test results. Table(4)

The results revealed that all the three brands of Mefenamic Acid complying with the B.P. 2003(95 to 105%). Table (11)
4.2 Conclusion:

The results obtained for these drugs using titration or UV-Spectrophotometric method revealed that they are stable and with good % content ranging between (95 to 105 % B.P,2003) for the three brands of Mefenamic Acid tablet although ; the brand B showed low percentage (95.87%), but ,they still remain between the accepted limits . It is important to conduct follow-up evaluation of these drugs to ensure that their content doesn’t fall below the accepted limits during their shelf-life.

The advantages of the developed method over official B.P method is use methanol which is the universal solvent suitable for polar and some of non polar drugs, cheap and available.

4.3 Recommendations:

Combating counterfeiting of medicines is a shared responsibility to which all interested parties have to contribute. At a global level a more effective response to the threat of counterfeit drugs could be the development of an international convention to control trade in counterfeit and substandard drugs .The high price of some drugs is not always an indication of top quality.

Bioequivalence studies should be conducted to ensure efficacy, quality and safety of drugs.
References:


