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Editorial

We start this pioneering work, which do not seek perfection as much as aiming to provide a scientific window that opens a wide area for all the distinctive pens, both in the University of Sabratha or in other universities and research centers. This emerging scientific journal seeks to be a strong link to publish and disseminate the contributions of researchers and specialists in the fields of applied science from the results of their scientific research, to find their way to every interested reader, to share ideas, and to refine the hidden scientific talent, which is rich in educational institutions. No wonder that science is found only to be disseminated, to be heard, to be understood clearly in every time and place, and to extend the benefits of its applications to all, which is the main role of the University and its scholars and specialists. In this regard, the idea of issuing this scientific journal was the publication of the results of scientific research in the fields of applied science from medicine, engineering and basic sciences, and to be another building block of Sabratha University, which is distinguished among its peers from the old universities.

As the first issue of this journal, which is marked by the Journal of Applied Science, the editorial board considered it to be distinguished in content, format, text and appearance, in a manner worthy of all the level of its distinguished authors and readers.

In conclusion, we would like to thank all those who contributed to bring out this effort to the public. Those who lit a candle in the way of science which is paved by humans since the dawn of creation with their ambitions, sacrifices and struggle in order to reach the truth transmitted by God in the universe. Hence, no other means for the humankind to reach any goals except through research, inquiry, reasoning and comparison.

Editorial Committee

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Publication instructions

The journal publishes high quality original researches in the fields of Pure Science, Engineering and Medicine. The papers can be submitted in English or Arabic language through the Journal email (jas@sabu.edu.ly) or CD. The article field should be specified and should not exceed 15 pages in single column.

All submitted research manuscripts must follow the following pattern:

- Title, max. 120 characters.
- Author Name, Affiliation and Email
- Abstract, max. 200 words.
- Keywords, max. 5 words.
- Introduction.
- Methodology.
- Results and Discussion.
- Conclusion.
- Acknowledgments (optional).
- References.

Writing Instructions:

Papers are to be submitted in A4 (200×285 mm) with margins of 25 mm all sides except the left side, which should be 30 mm. Line spacing, should also be 1.15.

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Invitation

The Editorial Committee invites all researchers "Lectures, Students, Engineers at Industrial Fields" to submit their research work to be published in the Journal. The main fields targeted by the Journal are:

- Basic Science.
- Medical Science & Technology.
- Engineering.

Refereeing

The Editorial Committee delivers researches to two specialized referees, in case of different opinions of arbitrators the research will be delivered to a third referee.

Editorial Committee

CONTENTS

STUDY OF THE ACTIVE INGREDIENT OF FOUR DIFFERENT BRANDS OF COMMERCIAL DICLOFENAC SODIUM OF SELECTED PHARMACIES IN THE WESTERN REGION OF LIBYA

Mustafa Benamer[1*], Areej Tabon[2], and Mohamed Alfrah[3]

[1,2,3] Department of Medicinal Chemistry, Faculty of Pharmacy/University of Zawia, Libya
[*] m.benamer@zu.edu.ly

Abstract

Diclofenac is a commonly used nonsteroidal anti-inflammatory drug (NSAID) in medical applications for the treatment of many diseases. The objective of this study is to determine the active ingredient of four brands of diclofenac sodium in the selected pharmacies in the western part of Libya to choose the best one. By comparison of the active ingredients of four different brands of diclofenac sodium (Olfen, Votrex, Emifenac, and Diclofenac Stada) has not been made available in public medical stores and pharmacies of Zawia, Libya. The study is based on the ultraviolet absorbance maxima at about 305nm wavelength of diclofenac sodium using a mixture solvent of water and ethanol. The solutions were scanned at the 200-400nm UV region. The wavelength maxima (λ_{max}) was observed at 305nm, and this wavelength was adopted for absorbance measurement. In general, most of the studied available brands' drug was within the specified standard range of 40-50 mg except the Emifenac brand.

Keywords: Diclofenac; active ingredient; UV-spectrophotometer; brand.

Introduction

Many generic versions of diclofenac tablets and injections by different manufacturers and from different countries exist today in Libya need to investigate their active ingredients and compare them to the pharmacopeial reference standards. In recent years, most of the products of diclofenac have become available in the market at different prices. However, variable clinical responses to these drug products from different manufacturers have been documented. These responses may be due to active ingredients, excipients, formulation process, and storage conditions.

According to the FDA, 2017, active ingredients are any chemical compounds or components in medicine that provide a pharmacological activity or other direct effects on a function of the body to treat a condition. Many medicines have the same active ingredients but are made by different companies and have different brand names (DHAC, 2023).

Diclofenac sodium is one of the medicines that is a well-known active substance with established efficacy and tolerability. It is a derivative of phenyl acetic acid and is commonly known in the form of sodium salt as Voltaren. According to the IUPAC name, it is known as sodium; 2-(2, 6-dichloroanilino) phenyl acetate. The molecular weight is 318.13 g/mol with the chemical formula ($C_{14}H_{10}Cl_2NNaO_2$), and it has the following structural formula Figure (1) (Todd and Sorkin, 1988).

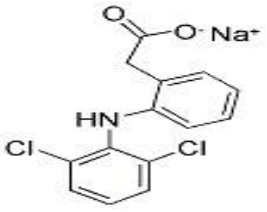

Figure (1): Molecular Structure of Diclofenac Sodium.

For physical properties, diclofenac sodium is white to off-white, odorless, crystalline, and slightly hygroscopic, soluble in water, sodium hydroxide, alcohol, acetone, and phosphate buffer. It is insoluble acid cyclohexane, chloroform, and acetonitrile. Melting Point is 283- 285°C (Salt) and 156-158°C (Free Acid). The n-octanol/water partition coefficient is 13.4 at pH 7.4 and 15.45 at pH 5.2. Its dissociation constant (pKa) is 4.0 ± 0.2 at 25°C in water (Dubois et al., 1998).

Diclofenac sodium 50 mg is the sodium salt form of diclofenac, a phenyl acetic acid derivate that contains the active ingredient and inactive ingredients (Vane, 1971). The inactive ingredients in Voltaren include hydroxypropyl methylcellulose, iron oxide, lactose, magnesium stearate, polyethylene glycol, etc. It is commonly used to relieve signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis of inflammatory, chronic (e.g. rheumatoid arthritis), and acute (e.g. headache) pain conditions, especially where there is an inflammatory element (Lesney, 2004; McCarberg; Gibofsky, 2012; Novartis, 2014).

Diclofenac sodium is completely absorbed after its passage through the stomach. Following ingestion of one tablet of diclofenac with or after a meal, it is slower than when it is taken before a meal, but the amount of active substance absorbed remains the same (Riess et al., 1978; Clarke and Moffat, 1986). It is well absorbed orally, 99% protein binding metabolized (in the liver), excreted both in urine (65%), and bile (35%), with a plasma half-life of 1 to 2 hours (Ishikawa and Herschman, 2007).

For the mechanism of action, the action of the single dose of diclofenac sodium is much longer (6 to 8 hours) compared to the short half-life that the drug indicates. This could be partly due to a particularly high concentration achieved in synovial fluids.

The exact mode of action is not well understood, but the primary action of NSAIDs is to inhibit the activity of the cyclooxygenase enzymes (Cox1 and Cox2) that oxygenate arachidonic acids into inflammatory prostaglandin. In most of the vertebrate species studied, two isoforms have been found (Martindale, 1996).

Diclofenac sodium's potential for toxicity is associated with polymorphisms of the cytochrome P450 gene family, which affects the patient's potential for drug metabolism. The common diclofenac side effects may include indigestion, gas, vomiting, stomach pain, nausea, diarrhea, headache, constipation, stuffy nose, drowsiness, increases in blood pressure, swelling, or pain of arms, and legs, and hair loss or eczema (Smolinske, 1990).

By researching in the literature review of Libya, there is no data about the determination of active ingredients of diclofenac sodium. Studies have been reported for the determination of diclofenac sodium by U. V spectrophotometry around the world, (Sastry et al., 1989; Agrawal; Shivramchandra, 1991; Patricia et al., 1999; 17. Ayorinde et al, 2012), visible spectrophotometry, thin layer chromatography, gas-liquid chromatography, HPLC, NMR, gas chromatography, and mass spectrometry.

Materials and Methods

The materials and methods outline the research methodology involved in field tests, laboratory analysis, and experimental methods. In this study, the analyzed parameter is the determination of the active ingredient of Diclofenac sodium available brands by UV spectrophotometric.

Collection of Samples

Four brands of Diclofenac Sodium tablets were obtained from various pharmacies in the western region of Libya. Samples were properly checked for their, Manufacturer's name, physical appearance, Batch number, Date of manufacturing, and Expiry date before purchasing. The labeled active ingredient of Diclofenac Sodium was 50 mg and packaged in a strip or blister Table (1).

Table (1): The Brand Name of Diclofenac Sodium and Manufactured Country.

Brand Name	Weight (mg)	Manufacture Date	Expiry Date	Manufactured Country
Olfen	50	10/2016	11/2018	Switzerland
Votrex	50	11/2015	11/2019	Jordan
Emifenac	50	06/2014	06/2017	UAE
Diclofenac Stada	50	02/2017	02/2020	Turkey

Apparatus

A Jenway 625, UV-visible spectrophotometer with 1.00 cm glass cells was used for the concentrations of diclofenac sodium in the studied brands. All absorbance measurements were carried out at room temperature.

Chemicals and Reagents

All the chemicals used in this study were of analytical reagent grade. For the preparation of the solutions and samples, deionized water and grade "A" glassware was used throughout. The solvent used was ethanol from (Breckland Scientific, UK) was used to prepare the samples.

Preparation of Standard Stock Solution

The best method for preparing the standard stock solution is to use standard diclofenac sodium. Unfortunately, this was not available, so the diclofenac sodium brand (Olfen) was used for this purpose. About 200mg (10 tablets) of diclofenac sodium (Olfen) was dissolved in hot water and some drops of ethanol for the preparation solution, then filtered the solution was by vacuum, transferred to a volumetric flask, and sufficient water to produce 500mL.

Preparation of Calibration Curve

Aliquots of standard solutions of diclofenac sodium (1, 2, 3, 4, and 5 ml) were transferred in a series of 50 ml volumetric flasks. The volume was adjusted to the mark with a mixture of distilled water and ethanol. The solutions scanned in the 200-400nm UV region. The wavelength maxima (λ_{max}) was observed at 305nm, and this wavelength was adopted for absorbance measurement.

Table (2): Data for Calibration Curve of Diclofenac Sodium.

Sr.No.	**1**	**2**	**3**	**4**	**5**
Conc (ppm)	10	20	30	40	50
Abs	0.15	0.32	0.45	0.57	0.69

The calibration curves were plotted over the concentration range10-50 ppm as shown in Figure (2), and the resulting regression equation is as follows $Y = 0.0138x + 0.0176$, $R^2 = 0.995$.

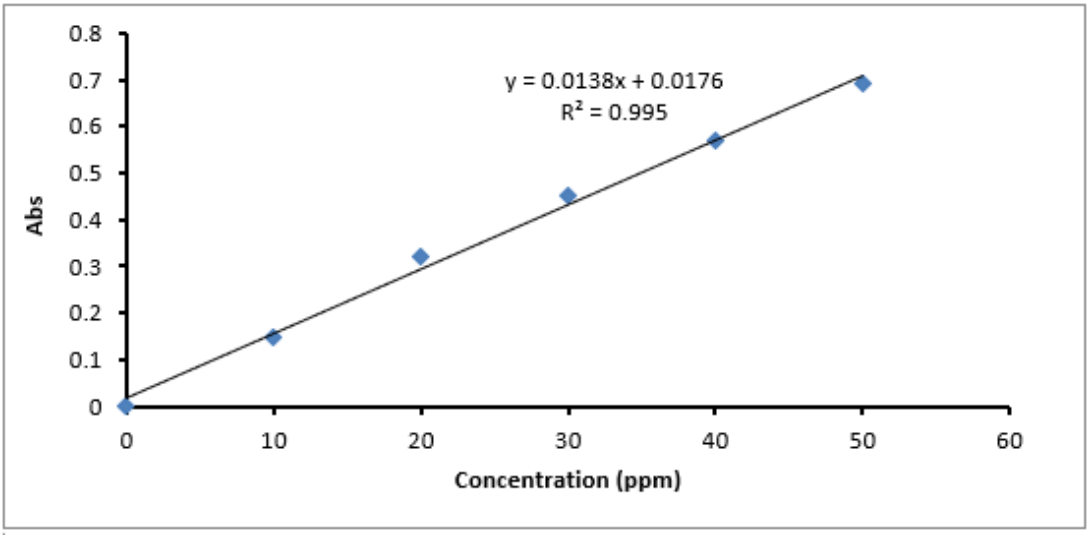

Figure (2): Calibration Curve of Diclofenac Sodium at 305nm.

Preparation of Samples

The four different brands (Olfen, Votrex, Emifenac, and, Diclofenac stada) were purchased from different pharmacies to determine the active ingredient of Diclofenac sodium. All of the tablets of each brand were weighed and placed in a mortar and ground to a fine powder. An amount of the powders equivalent to 50 mg of pure diclofenac was accurately weighed and dissolved in a minimum volume of ethanol. The solution was stirred for 15 minutes and then made up of 50 ml of hot deionized water and some drops of ethanol. The solution was filtered using the vacuum system, transferred to a volumetric flask, and added sufficient water was to produce 100mL. The precision of the instrument was checked by repeated scanning and measuring the absorbance of solutions (n= 3) of diclofenac sodium.

Analysis of Samples

After the preparation of standard and tablet solutions, the strength of solution100 ppm in 10 ml absorbance of the sample preparation and standard preparation in a 1cm cell at the wavelength of maximum absorbance at about 305 nm, using a spectrophotometer, using the blank solution. Calculate the quantity in mg, of diclofenac sodium per tablet.

Results and Discussion

The results that were obtained from the experiments are presented in the form of tables with some explanations. The most important findings of this study are also discussed in this chapter. The study carried out the pharmaceutical determination using a spectrophotometer on all brands of diclofenac sodium tablets. Table (3) shows the name brand and concentration of different brands. For data analysis, the obtained results are reported in terms of 95% Confidence Intervals (±).

Table (3): Absorption and Concentration Values (± Confidence Intervals).

Brand name	Wt of tablet	Absorbance at 305nm	Concentration (mg/l)
Stada	50mg	0.645	45.66±0.54
Votrex	50mg	0.534	42.25±0.61
Emifenac	50mg	0.378	29.54±0.91
Olfen	50mg	0.777	49.82±1.21

In this study, the active ingredient diclofenac sodium was investigated in four types different in manufacturing countries (Turkey, UAE, Jordon, and Switzerland) and the same type of dosage forms (tablets).

Our results reveal that among all four brands of diclofenac sodium (Olfen, Votrex, Emifenac, and Diclofenac Stada). Olfen brand showed the highest concentration of 49.82 mg while Emifenac showed the lowest concentration level of 29.54mg. Stada, and Vortex brands also showed a high concentration of 45.66 and 42.25 mg respectively Figure (3). The diclofenac concentrations in the three brands of Olfen, Votrex, and Stada were significantly higher than those in the Emifenac brand.

Since there are no studies for the active ingredient of diclofenac sodium in Libya, the results were compared with previous studies around the world. The obtained diclofenac concentrations quietly concurred with the finding range of 35-49 mg from Sastry et al., 1989; Agrawal; Shivramchandra, 1991; Patricia et al., 1999; and Ayorinde et al, 2012.

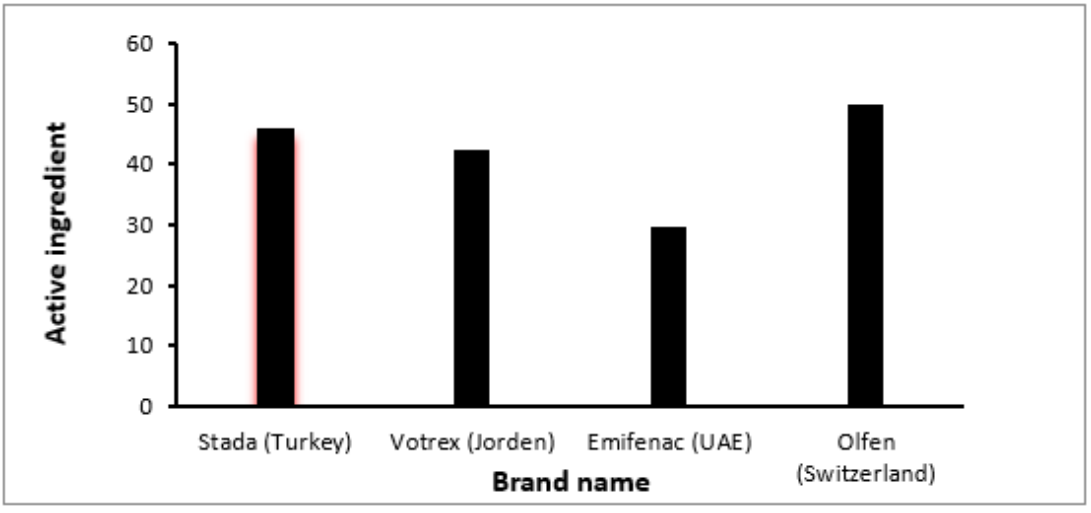

Figure (3): The Active Ingredient for Different Brands of Diclofenac Sodium.

Conclusions

By comparing the results, the best brand was Olifen tablets followed by Stada and Votrex tablets, while Emifenace tablets were the worst. The result also showed that all of the four brands are close to the allowed concentration of 50mg except Emifenace tablets. This study confirms the need for constant surveillance of pharmacies within Libya to ensure that commercially available drugs in pharmacies are confirmed with the pharmacopeial standards. It is important to conduct a follow-up evaluation of these drugs to ensure that their content doesn't fall below the accepted limits during their shelf-life.

Recommendations

The obtained results should be used in future research to assess the bioavailability of Diclofenac sodium. Quality control testing of Diclofenac sodium tablets should also be studied.

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