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Review Article

A review: Determination of Diclofenac Sodium in Certain Pharmaceutical Preparations by Spectrophotometric and Chromatographic Methods

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ABSTRACT

Diclofenac is act as analgesic and antipyretic drug, known as voltarol, voltarine, dicloflex, and many other known brand names, formulated mainly as capsules and tablets, or as gel and suppositories. Spectrophotometric methods for determination of diclofenac were based on oxidation-reduction reaction or on complex -formation reactions, as well as determination based on UV - derivatives detection, first or second order. Many HPLC-methods for determination of DFC have been published, these methods use different dimensions C_{18} columns and different compositions of mobile phases, acetonitrile is one of the major components of mobile phase because it offers a suitable polarity and viscosity, few procedures use the internal standard, while many of the selected review articles involve detection by UV-detector. Many other determination methods have been published, this review concern on the spectrophotometric and chromatographic methods. The aim of the review is to offer these reported methods to analysts to be in use for quality control of the dosage forms, and to use the selected procedures for new work to determine other related compounds.

Keywords: Analytical methods, diclofenac, pharmaceutical preparations, review.

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INTRODUCTION

Diclofenac (DFC) is a non-steroidal, decreases inflammation, used to treat rheumatoid arthritis cases, musculoskeletal injuries, and osteoarthritis (Pawel *et al*., 2021; Altman *et al*., 2015). It also exhibits an analgesic property as post-surgery analgesia (Bilal and Ulvihan, 2015). It is phenylacetate salt with the empirical formula $C_{14}H_{10}C_{l2}NO_2Na$ and chemical structure as in Fig. (1):

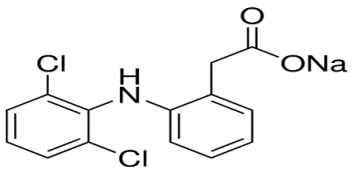


Fig. 1: The chemical structure of diclofenac sodium (Wilson *et al*., 2004)

DFC is soluble at 25°C in water (9 mg/ml); this ratio is varied according to the pH of the solution as shown in Fig. (2), while the dissolution in methanol is higher than 9 mg/ml, in acetone is 6 mg/ml, in acetonitrile is less than 1 mg/ml, and in cyclohexane is less than 1mg/ml (Moffat *et al*., 2011), a spontaneous ion-association of DFC in aqueous -methanol mixture is occurred (Hakam and Al-Tamer, 2022).

DFC exhibits maximum absorbance at 282nm in methanol (Ragini *et al*., 2019), and 273 nm in aqueous acid (Moffat *et al*., 2011) as shown in Fig. (3). DFC can be synthesized by three different paths, but the reaction begging with 1,5-dichloro aniline and chlorobenzene is the easier one (Alberto *et al*., 2021), scheme 1 show the synthesis reaction of DFC.

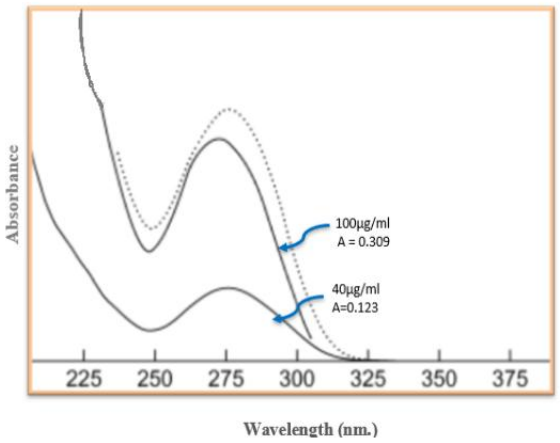


Fig. 2: The solubility of DCF in standard DFC different medium

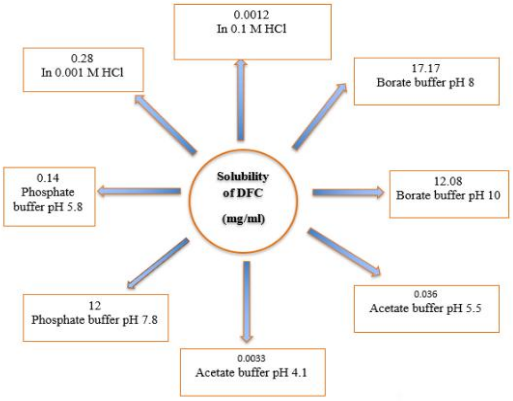
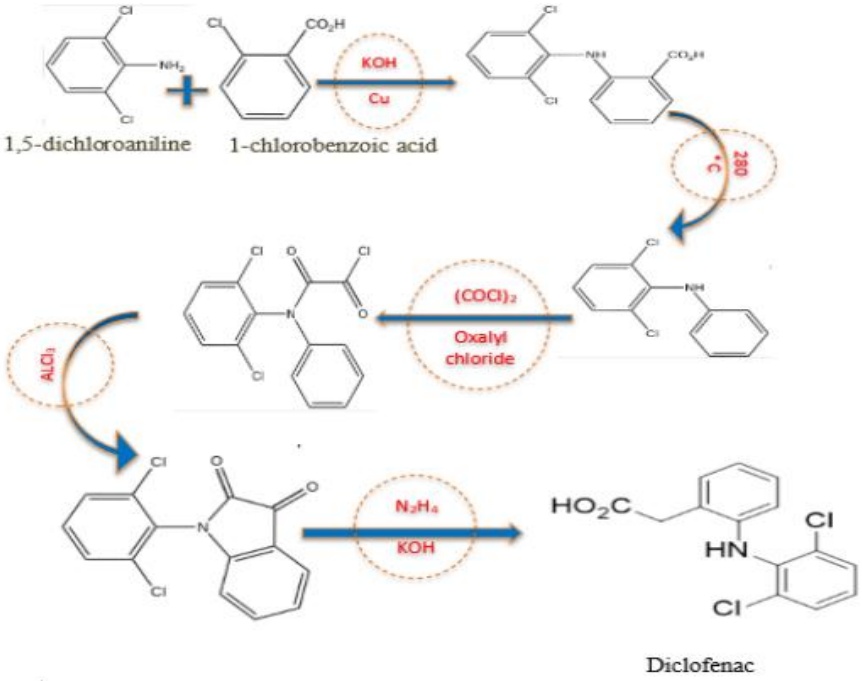


Fig. 3: Absorption spectrum of solution in aqueous acidic medium



Scheme 1: The organic synthesis of DFC begging with 1,5-dichloro aniline and chlorobenzene (Alberto *et al*., 2021)

Spectrophotometric methods for the estimation of DFC in dosage forms

An oxidation of DFC by ferric was used to assay DFC, the produced ferrous ions reacts with O-phenanthroline (El-Didamony and Amin**,** 2004) or by concentrated nitric acid (63% w/v) to form a yellowish compound measured at 380 nm. (Matin and Jouyban, 2005) oxidation by ferric and reaction with potassium hexacyanoferrate has been also used to assay DFC by spectrophotometry at 710nm. (Abdul Barry and Mohammed, 2009). The principle of oxidation of DFC has been used in other way. In bleaching reaction, DFC oxidized by an oxidizing agent, the exceed amount of the selected oxidizing agent such as cerium (IV) bleach the color of methyl orange which exhibits maximum absorbance at 470 nm (Nagaraju and Kanakapura, 2016).

Chemically the structure of DFC shows the ability of the compound to act as complexing agent, therefore some determination procedures were based on the formation of chelate with copper (II) at pH 5.3 to produce green complex measured at 680 nm (Rafael *et al*., 2005). A cobalt – DFC complex has been followed kinetically at 376 nm. (Snezana *et al*., 2007). The complexation reaction of DFC with cupric chloride and cobaltous chloride has been followed by atomic absorption via determination of copper and cobalt content, the assay requires acid digestion and dichloromethane extraction (Sunil and Sandeep, 2010).

UV partial least squares measurements has been adopted in the presence of 15 different excipient act as interfering additives (Marcelo *et al*., 2004). Derivative spectrophotometry of DFC at 249 nm. offers a specific estimation in water (Vishruti *et al*., 2013), and in acidic methanol at 273nm. (Gulshan, 2013). The effect of interferences in DFC dosage forms has been eliminated by first order spectrophotometric derivative at 258 nm after dissolution in NaOH (1M) (Saad *et al*., 2018). A UV method for determination of DFC based on the 2nd derivative at more critical wavelength 264.20 nm. has been determine DFC in marketed dosage form (Kinjal *et al*., 2019).

High-performance liquid chromatography methods for estimation of DFC in dosage forms

As the chemical structure of DFC involve many polar functional groups, therefore, C_{18} column is the suitable packaging column for separation of DFC from excipients contaminates, or components. while the affinity of DFC to the stationary phase and subsequent elution with mobile phase require a balance between the variables of polarity of mobile phase, already neither strong

acidic nor strong basic solutions cannot be used to avoid the damage of the column (Nabeel *et al.*, 2011). Therefore, buffers can be used to justify the elution medium. Orthophosphoric acid and acetonitrile were used as the mobile phase to elute DFC flowing at rate of two milliliter per minute, and measuring at 210 nm. (Bushra, 2019). A relatively polar mobile phase consists of (30:70% v/v) formic acid: acetonitrile flowing in one milliliter per minute and detecting at 275 nm has been used by researchers to determine DFC (Prasanna *et al*., 2019). DFC as solid dosage forms of Ninava State Company for Drug Industries and Medical Appliances has been determined by HPLC method and eluted by the mobile phase consists of methanol, deionized water and acetonitrile in the ratio of 60:20:20 respectively (Riyadh, 2012). As the pre-reviewed solubility of DFC chromatographic criteria of it, many mobile phases consist of buffered solution of phosphate at many ratios with either methanol (Madhuri, 2016). or acetonitrile (Sonali *et al*., 2018). As it may be consisting of acetate buffer and methanol passing into a specific SB-C7 column (Mohammed *et al*., 2020). The stability of prepared emulsion of DFC has been followed by HPLC method at 276 nm. using Hypersil BDS, which eluted by unbuffered acetonitrile: methanol mixture (Shiv *et al*., 2013).

Other analytical methods used for estimation of DFC in dosage forms

Many other techniques have been used for the estimation of DFC, an amperometric method of DFC after batch injection criteria has been published, the method exhibits high precision in which the relative standard deviation was 1.1% also 1.1 μmol L^{-1} was the detection limit ,the same research explain a capillary electrophoresis procedure for determining DFC in pharmaceutical preparations and exhibits 95% confidence when compared with HPLC method for determination of the same drug formulation (Denise *et al*., 2013). Sweep voltammetry - coupled with gas chromatography and mass spectrometric detection has been used for estimation of DFC in pharmaceutical preparations without any interfering effect of excipients in the drug, the method show high sensitivity and good suitability for the quality control of DFC dosage forms (Bilal and Ulvihan, 2015). The assay of DFC has been improved by the principle of immobilization of DFC via its amine group on the surface of carboxylic acid groups of carbon multi-wall nanotube (Yi *et al*., 2022). Different methods and techniques have been determining DFC in biological samples these require higher sensitivity and of course higher selectivity (Szpot *et al*., 2021) (Dang *et al*., 2021).

CONCLUSION

Diclofenac is drug of wide range treat of pain, can be synthetic in the laboratory by reaction of 1,5-dichloro aniline with chlorobenzene, its solubility in aqueous medium increase with increases the alkalinity, and can be identified at 277nm in acidic solution. DFC can be determined easily by direct or indirect spectrophotometric methods, chromatographic methods provide higher sensitivity for determining of DFC, and the hyphenated techniques provide higher selectivity for determining of DFC.

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تقدير الدكلوفيناك صوديوم بالطرائق الطيفية والكروماتوغرافية فى المستحضرات الصيدلانية

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الملخص

يستخدم الديكلوفيناك بوصفه عقار مسكن وخافض للحرارة ويعرف تجاريا بأسماء كثيرة منها ديكلوفليكس وفولتارين وفولتارول وغيرها. ويأخذ الديكلوفيناك الاشكال الدوائية المختلفة ومنها الأقراص والكبسولات وكذلك الجل والتحاميل. تعتمد طرائق التقدير الطيفية للديكلوفيناك على تفاعلات الاكسدة والاختزال او تفاعلات تكوين المعقدات كما تعتمد بعض الطرائق الطيفية على متابعة الدواء في منطقة طيف الاشعة فوق البنفسجية وعلى اخذ طيف المشتقة الأولى او الثانية. في حين تعتمد كثير من الطرائق الكروماتوغرافية ضمن تقنية كروماتوغرافيا السائل عال الأداء على استخدام عمود فصل بأبعاد مختلفة ولكنها غالبا ما تكون متقاربة كما وتشتمل على استخدام طور متحرك متعدد المكونات ومختلف النسب يعد الاسيتونتريل أحد اهم هذه المكونات لكونه يمتلك قطبية ولزوجة مناسبتين. بالرغم من وجود طرائق مختلفة لتقدير الديكلوفيناك الا ان هذه المقالة تناولت الطرائق الطيفية والكروماتوغرافية بشكل خاص. ان الهدف من هذه المقالة هو عرض طرائق التقدير هذه لتكون في متناول المحللين الكيميائيين لاستخدامها في متابعة محتوى مستحضرات الديكلوفيناك من المادة الفعالة وللاستفادة من الطرائق المذكورة ضمن هذه الدراسة لتقدير ومتابعة مركبات دوائية أخرى في مستحضراتها الصيدلانية.

الكلمات الدالة: طرائق تحليلية، ديكلوفيناك، مستحضرات صيدلانية، مراجعة.