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ORIGINAL ARTICLE

Spectrophotometric determination of some analgesic drugs in pharmaceutical formulations using N-bromosuccinimide as an oxidant

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Abstract New sensitive and rapid spectrophotometric methods for the determination of four analgesic drugs namely, nalbuphine (NALB), naltrexone (NALT), morphine (MORF) and tramadol (TRAM) in pharmaceutical formulations were developed and optimized. The proposed methods involve the addition of a measured excess of N-bromosuccinimide in acid medium followed by determination of unreacted NBS by reacting with either a fixed amount of methyl orange and measuring the absorbance at 508 nm (Method A), or orange G and measuring the absorbance at 478 nm (Method B). In both methods, the amount of NBS reacted corresponds to the amount of drugs. Under the optimum conditions, Beer's law limit, molar absorptivity and Sandell's sensitivity were calculated. The limits of detection and quantification were also reported for both methods. Statistical evaluation of the methods was examined by determining intra-day and inter-day precisions. The methods were successfully applied to the assay of drugs in their pharmaceutical formulations. No interference was observed from common additives and the validity of the methods was tested.

1. Introduction

Nalbuphine (−)-17-(cyclobutylmethyl)-4,5α-epoxymorphinan-3,6α,14-triol (Fig. 1a) is a semisynthetic narcotic agonist–antagonist of the phenanthrene series. Structurally, it is closely related to naloxone, an antagonist of the opiate receptors and to oxymorphone, a narcotic agonist. Nalbuphine has been shown to be approximately equianalgesic to morphine, yet with a ceiling effect on ventilator depression and fewer adverse effects than pethidine or pentazocine. As an analgesic agent, it is almost as potent as morphine and has been widely used in the treatment of acute and chronic pain (Pick et al., 1992). Its main advantages over morphine are a ceiling effect of respiratory depression, low tolerance liability and a lack of significant withdrawal symptoms. It is available as an injection for intramuscular and intravenous administration. The usual recommended doses are 10–20 mg by intravenous or intramuscular injection every 3–4 h. As to our best knowledge, there is no official analytical method for analyzing NALB in ampoule, in pharmacopoeias and the literatures.

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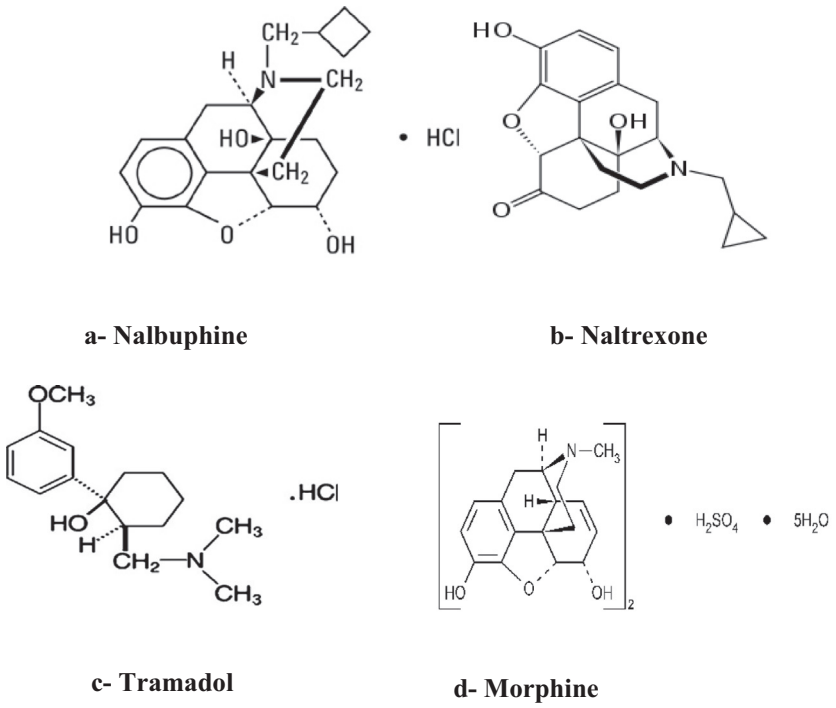

Figure 1 Chemical structure of the selected drugs.

A few methods have been described to detect nalbuphine in pharmaceutical formulations and in biological fluids; they include gas chromatography coupled to electron-capture detection (Weinstein et al., 1978), or mass spectrometry (Yoo et al., 1995), high-performance liquid chromatography with electrochemical detection (Groenendaal et al., 2005; Pao et al., 2000) and LC–MS/MS (Cai et al., 2011). The GC methods (Yoo et al., 1995), although sensitive, involved expensive equipment and time consuming preparation of samples and are not easily available for routine drug monitoring.

Naltrexone (17-cyclopropylmethylmethyl-6-deoxy – 7,8 – dihydro-14-hydroxy-6-oxo-17-normorphine) (Fig. 1b), is a long-acting synthetic opiate antagonist with few side effects that is efficacious when administered orally, either daily or three times a week for a sustained period of time. Naltrexone has been determined by using a wide variety of analytical techniques, particularly chromatographic, such as high-performance liquid chromatography (HPLC) with electrochemical detection (Brünen et al., 2010), liquid chromatography (Slawson et al., 2007), and gas chromatography coupled with mass spectrometry (Mehrdad et al., 2009).

Tramadol hydrochloride is a centrally acting analgesic, used for treating moderate to severe pain. Tramadol hydrochloride possesses agonist actions at the μ-opioid receptor and effects reuptake at the noradrenergic and serotonergic systems. Tramadol is a compound with μ-agonist activity. Chemically it is [2-(dimethylaminomethyl)-1-(3-methoxyphenyl) cyclohexanol)], (Fig. 1c). It is used to treat moderate to moderately severe pain and most types of neuralgia, including trigeminal neuralgia. The BP (British Pharmacopoeia, 2003), specifies the non-aqueous titration technique detecting the end point potentiometrically for the determination of tramadol and dothiepin hydrochlorides while acebutolol was assayed in aqueous medium using 0.1 M NaOH titrant. Because of its wide use, several techniques have been reported for its assay in biological and pharmaceutical samples that include a number of high-performance liquid chromatographic (HPLC) (Chandra et al., 2012; Saccomanni et al., 2010), electrochemical (Garrido et al., 2003), potentiometric methods (Ganjali et al., 2008; Abu Shawish et al., 2011), and amperometry (Malongo et al., 2008), voltammetry (Ghorbani-Bidkorbeh et al., 2010), and flow injection chemiluminescence spectrophotometry (Zhang et al., 2009). The literature reported three spectrophotometric methods differed from our described work (Anis et al., 2011; Abdellatef et al., 2006).

Morphine (5α,6α-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol) (Fig. 1d), is a therapeutic drug that is used commonly for the control of pain and also abused as an illicit drug. It is recommended by the World Health Organization (WHO) for the relief of moderate cancer-related pain. Moreover, heroin is hydrolyzed in the organism to morphine; therefore, the determination of morphine content of biological samples is helpful for clinical and forensic purposes (Hoffman et al., 1997). However, it is toxic in excess and when abused. To prevent overdose-induced toxication, it is necessary to sensitively monitor the concentrations of morphine in a patient's blood or urine. Various analytical methods have been developed for the determination of morphine and its major metabolites. The most common analytical techniques currently used include gas chromatography (Matyus et al., 2012; Barroso et al., 2010), high-performance liquid chromatography (Berga et al., 2009; Ruzilawati et al., 2012), and their combination with other detection methods, capillary electrophoresis (Mi et al., 2004), chemiluminescence (Francisa et al., 2008), voltammetric (Ali et al., 2011; Li et al., 2009), and electrochemical (Li et al., 2010). To the best of our knowledge, only a report