Spectral Studies of Analgesic, Antipyretic and Anti-Inflammatory Drugs Used in Medical Therapy in Romania

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Abstract

Human health decline is most commonly manifested by pain and sometimes fever in the initial phase of the disease. Analgesics, antipyretics and anti-inflammatories serve as drugs with various chemical structures which showcase in different proportions their main actions. They represent medicines that suppress pain and fight fever. The aim of the paper is studying the usual types of therapeutic indications using modern spectral analysis, based on the analgesic, antipyretic and anti-inflammatory actions. The following spectral analysis methods are used to control the chemical compositions of the studied drugs: UV-VIS analyses and IR analyses.

Keywords: UV-VIS spectra, IR spectra, analgesic, antipyretic, anti-inflammatory.

Introduction

Analgesics and antipyretics are drugs that reduce or suppress pain and fight fever. They are a group of drugs with various chemical structure and have associated in different proportions the following main actions: analgesic, antipyretic and anti-inflammatory. Pain is an important alarm system in body protection [1, 2]. Triggers defense reactions to remove the harmful agent [2, 3]. Provides useful guidelines for diagnosis [4, 5]. Acute pain causes an increase in heart rate, heart rate and blood pressure, mydriasis, sweating, hyperventilation, mental anxiety [4]. It is possible to reduce or suppress pain, using drugs that act at different levels, on the links involved in the formation and conduction of nerve influx and in the perception of pain [3, 4]. To combat the pain you can intervene:

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1. Preventing the formation of nerve influx, in sensitive endings: local anesthetics, muscle relaxants, vasodilators, anti-inflammatory drugs.

2. Preventing the transmission of nerve influx through sensitive fibers - the case of local anesthetics.

3. Prevention of pain perception, at the level of integration centers: general anesthetics, antipyretic analgesics, morphinomimetic analgesics.

Analgesic - Antipyretic - Anti-inflammatory Actions

Antipyretic-analgesics act analgesically only at the talamus level, raising the threshold of pain perception, without influencing the reaction to pain. The analgesic effect, for some substances in this group, is more evident in somatic pain, localized and superficial (examples: neuralgia, arthralgia, headache), with or without an inflammatory component and is weaker in visceral pain, deep and generalized. In some cases, a peripheral, anti-inflammatory mechanism would be added to the central, thalamic mechanism [5, 6].

Antipyretic analgesics also influence the thermoregulatory center, without having any other effects on the CNS. They do not produce sedative effects, drowsiness and sleep. It does not affect other types of sensitivity and sensory functions. It has no peripheral effects on the digestive, respiratory, cardiovascular systems. Some analgesics-antipyretics have anti-inflammatory effect, [4, 7].

Antipyretic analgesics reduce the fever by acting on the thermoregulatory centers, they decrease their functional level by tending to restore it to normal values. As a result, peripheral vasodilation, sweating, and decreased metabolism occur. The substances have no effect when the thermoregulatory centers function normally, so they do not lower the normal body temperature, they are not hypothermic but only antipyretic [4, 8].

The action of analgesics-antipyretics on fever is nonspecific and occurs directly through the central mechanism. Fever can also be reduced by drugs that act specifically, but indirectly, on biological pathogens, for example by antibiotics and chemotherapeutics [8, 9].

In acute viral infections of the respiratory tract, analgesics - antipyretics are the medication of choice, in mild and moderate forms, uncomplicated, in patients who do not have organic suffering and in whom antibiotics and chemotherapeutics are not necessary. In infectious fevers with antibiotic-sensitive or chemotherapeutic germs, specific medication will be administered. Antipyretics are associated with them only in cases of high fever, with repercussions, on the CNS and cardiovascular system [1, 4, 8].

Qualification

Chemical structure is an important classification criterion. Thus we have [4]:

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Salicylic acid derivatives: Acetylsalicylic acid, Aspirin Direkt, Upsarin, Alka Seltzer

(effervescent) Lysine acetylsalicylate, Salicylamide, Diflunisal, Benorilate (acetylsalicylic acid ester with paracetamol)

Pyrazolone derivatives: Phenazone, Aminophenazone, Noramino-phenazone-Metamizole- (Algocalmin ampoules, Metamizole sodium suppositories, Algozone, Novalmin, Novalgin), Propiphenazone (Propiphenazone suppositories).

Aniline (p-aminophenol) derivatives: Phenacetin, Paracetamol (Paracetamol, Paracetamol suppositories, Efferalgan, syrup, or suppositories)

Quinoline derivatives: Glafenine

Non-narcotic analgesics are fundamentally different from morphinomimetic drugs, as they do not produce euphoria, tolerance, physical and mental dependence, so they do not cause drug addiction [5].

Therapeutic Indications

Analgesics-antipyretics have several types of therapeutic indications, based on analgesic, antipyretic, anti-inflammatory, antispasmodic actions. For each of these types of indications, the substances can be used either alone, in isolated administration or in combination, in complex formulas [4, 9÷ 11]. In principle, within the associations it is possible to achieve:

An additive effect, when substances from different chemical groups are used, but act on the same substrate. The advantage of the combination is that lower doses of each substance are used than in their case in isolation.

A potentiating effect, more effective than the previous one, when substances with action on different substrates are used.

Therapeutic indications based on analgesic action (sometimes with an anti-inflammatory component) Neuralgia (dental, intercostal, sciatica). Arthralgias (arthritis, osteoarthritis, spondylosis). Myalgias. Orthopedic disorders (sprains, dislocations, fractures). Postoperative pain. Headache. Dysmenorrhea, [10, 11].

Indications based on analgesic and antispasmodic actions Colic (renal, biliary), dysmenorrhea [4, 11].

Methods and equipment

The spectral method of analysis is one of the most widely used methods for obtaining data on the structure and chemical composition of medicinal substances [12÷15].

UV-VIS and IR spectral analysis methods are often used in drug control to obtain reliable data on the structure of compounds [13,14]. IR spectrophotometry is mainly used to identify drug substances without destroying the integrity molecules. IR absorption is characteristic of a wide range of functional groups, bonds, and structural

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units. Analyzed drugs by UV-VIS and IR techniques are: aspirin, paracetamol, nimesulide and sodium diclofenac.

UV-VIS spectroscopy

In the UV-VIS analysis spectra, a molecule absorption spectrum is obtained and the Lambert-Beer law is used to obtain quantitative data. Upon impact between a photon and a molecule, the photon undergoes either diffusion (an elastic shock without loss of energy) or absorption (it increases the internal energy of the molecule). Energy absorption occurs when the energy of the photon corresponds to the energy difference between two possible energy levels. The absorption spectrum of a substance is obtained by recording in a graph the variation of a quantity that characterizes the absorption of light (eg. extinction, absorbance, A, extinction coefficient ε, depending on the wavelength or number of waves, expressed in convenient units for the respective spectral domain [13÷15].

Minimum and maximums appear in the spectra thus obtained; the latter, called absorption bands, correspond to the regions of maximum absorption. The temperature can significantly influence the measured absorbance values. By observing this process with the help of a spectrophotometer is obtained an absorption spectrum of the molecule, that is, a representation of absorption as a function of frequency or wavelength. The Lambert-Beer Law is used to obtain quantitative data,

$$A = log\frac{I_0}{I} = \varepsilon cl \qquad \qquad \frac{I}{I_0} = T$$

$$(1) \qquad \qquad (2)$$

 where: A is absorbance, T is transmitance, I_0 and I are the intensities of light before and after the passage of a solution, ε is called the absorption coefficient or molar absorbability. c is the concentration of solution, l is the thickness of the analysis vessel.

The analysis equipment is the GBC Cintra 10e UV-VIS Spectrophotometer which has the   following characteristics: it is a double-beam UV-VIS spectrometer, with monochromator, with direct recording of the ratio of test and reference signals and very high scanning speed. Fully automated, it is controlled by an external computer.

IR spectroscopy

The infrared spectral range, IR, ranges from 780 nm to 300 nm, but a narrower range of 2.5 μm to 1.5 μm is used for analytical determinations. There are three areas in IR, namely near IR, middle IR, and far IR. For structural analyzes, including detection, only the average IR region is of interest, which provides the most analytical

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information. The near IR spectral range is less exact in specific information than the average one, being used mainly for quantitative determinations, and the far IR range is used only in research [13÷15]. IR spectrophotometry is mainly used for the identification of organic substances, including drugs, without destroying the integrity of molecules and less for dosing. IR absorptions are characteristic of some functional groups, bonds, and structural units that the IR spectrum can be thought of as a fingerprint of the molecule studied, which makes it easier to deduce structural details and recognize them. The Jasco IR 4200 Spectrometer Analysis Equipment has the following features: 7800-350 cm^{-1} wavelength range, single beam system, high intensity ceramic radiation source, DLATGS Detector (standard).

Results and discussion

Following the spectral analysis, we obtained the following results, which are systematized according to the method and technique of analysis that we used to obtain the spectra.

UV-VIS spectrum of aspirin

The range of ultraviolet in the visible spectrum is 200-350 nm. The UV-VIS spectra of aspirin in hydrochloric acid solution (0.1 N HCl) and in neutral solution are shown in Fig. 1. The maximum ultraviolet absorption of aspirin was found at 230 nm and 278 nm in acids (0, 1 N HCl) and 225 nm and 276 nm in the methanol solution. The results obtained for the spectra with the wavelength for maximum absorption of aspirin in the solvent-aspirin mixture were compared with the aspirin reference spectrum [10, 11, 15].
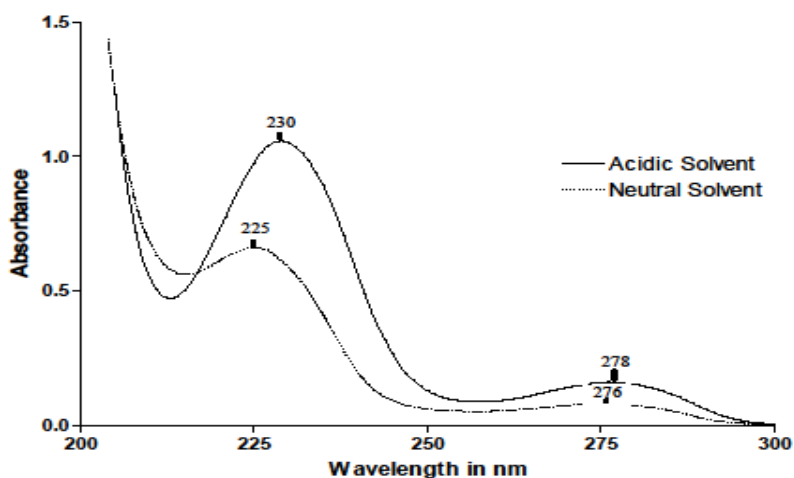

Fig. 1 UV-VIS spectrum of aspirin

The UV-VIS spectrum of paracetamol

The range of ultraviolet in the visible spectrum is 200-350 nm. The UV-VIS spectra in hydrochloric acid solution (0.1 N HCl), in alkaline solution (0.1 N NaOH) and in neutral solution are shown in Fig. 2. The molecular structure for paracetamol is shown in Fig. 2, also.
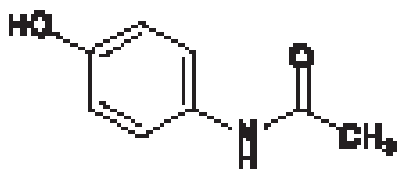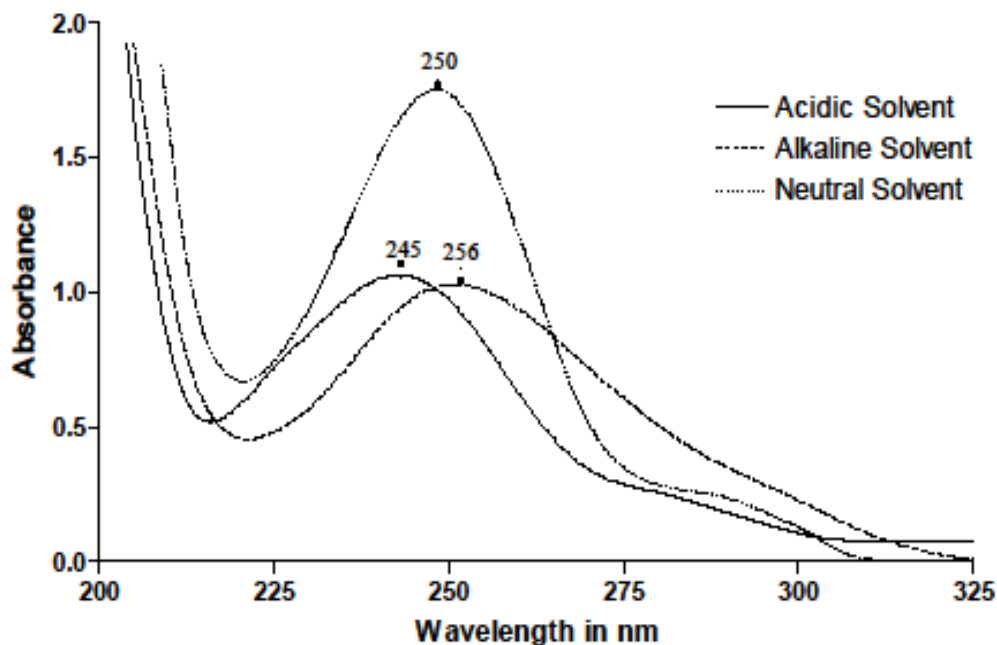

Fig. 2. UV-VIS spectrum and structure of paracetamol

The maximum ultraviolet absorption of paracetamol was found at walvelenghts 245 nm, 256 nm and 250 nm in acid solution (0.1 N HCl), in alkaline solution (0.1 N NaOH) and in neutral solution. The results obtained for the spectra with the maximum wave absorption in the acidic and alkaline solutions of the solvent-paracetamol binary systems were compared with the paracetamol reference spectrum [10,11].

UV-VIS spectrum of nimesulide

It is a non-steroidal anti-inflammatory drug (NSAID) with analgesic (pain relieving) properties. It is used to treat acute pain and painful osteoarthritis symptoms. The range of ultraviolet in the visible spectrum is 200-350 nm. Nimesulide's molecular structure and the UV-VIS spectra in acid solution (0.1 NHCl), in alkaline solution (0.1 N NaOH) and in neutral solution are shown in Fig. 3.
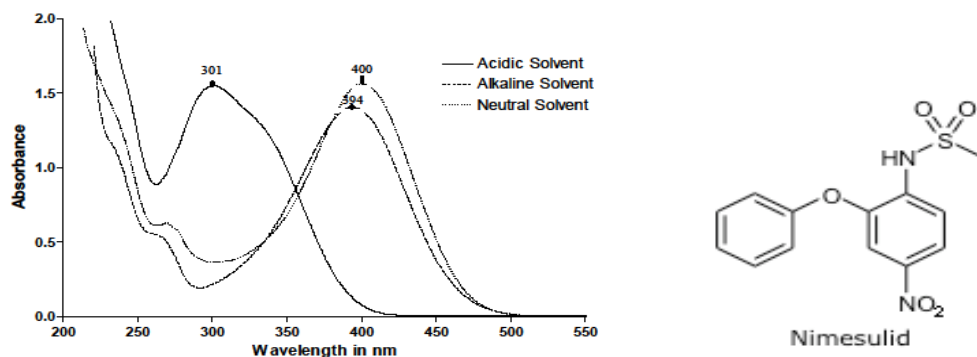

Fig. 3 UV-VIS spectrum and nimesulide structure

Ultraviolet absorption maxima of Nimesulide were found at walvelenghts 301nm, 394 nm and 400 nm in acid solution (0.1 N HCl), alkaline solution (0.1 N NaOH) and neutral solution, respectively. The results obtained for the spectra with the maximum absorption for nimesulide in the acid and alkaline solutions were compared with the nimesulide reference spectrum [10, 11].

UV-VIS spectrum of diclofenac sodium

The range of ultraviolet in the visible spectrum is 200-350 nm. The UV-VIS spectra of diclofenac sodium in acid solution (0.1 N HCl), in alkaline solution (0.1 N NaOH) and in neutral solution for solvent-diclofenac sodium binary systems are shown in Fig. 4. Maximum absorption of diclofenac ultraviolet was found at walvelenghts 273 nm, 275 nm, 279 nm in acidic (0.1 N HCl), alkaline (0.1 N NaOH) and neutral binary systems, respectively. The results obtained for the maximum absorption spectra were compared with the reference spectrum of diclofenac sodium [10, 11].
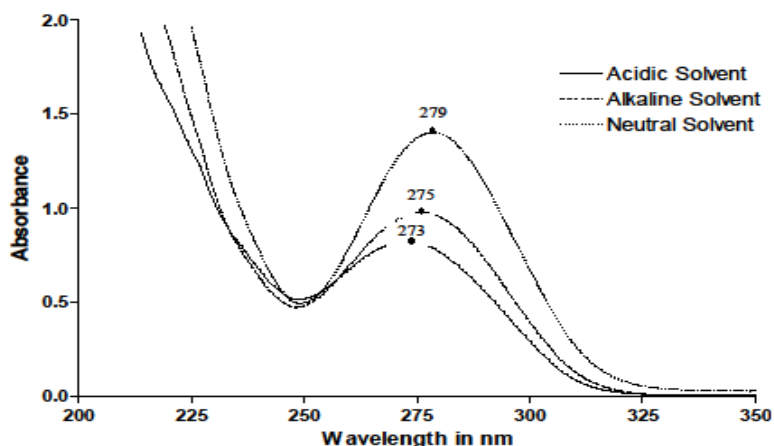
FIG. 4. UV-VIS spectrum of diclofenac sodium

IR spectrum of aspirin

The infrared spectrum of aspirin is shown in Fig. 5. The main wave numbers obtained in the infrared spectrum and their corresponding assignment (bond, type and combined functional group) were characteristic for aspirin. In the range 490 cm^{-1} - 1740 cm^{-1} are combined functional groups with transminttance under 65%T. At 2820 cm^{-1} a level of transmittance 85%T is recorded.
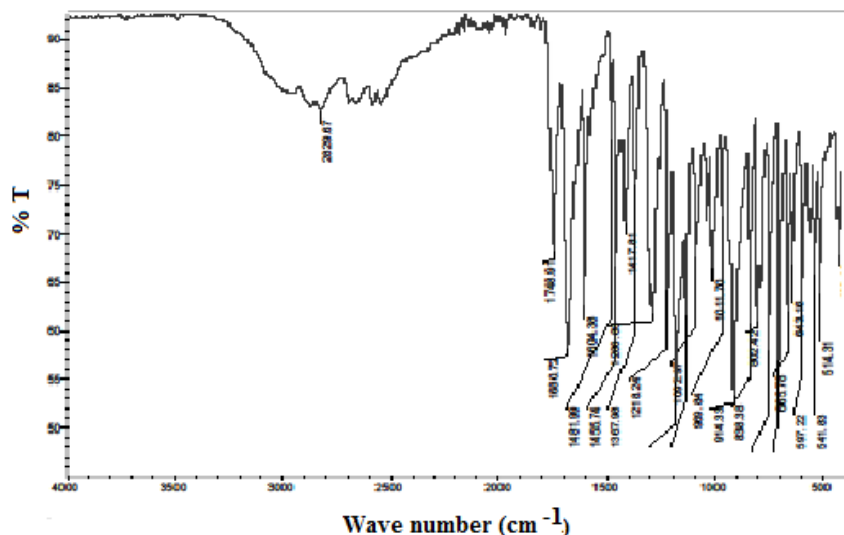

Fig. 5. IR spectrum of aspirin

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IR spectrum of paracetamol

The infrared spectrum of paracetamol is shown in Fig. 6. The main wave numbers obtained in the infrared spectrum and their corresponding assignment (bond, type and combined functional group) were characteristic of paracetamol. In range 484,2 cm^{-1} - 1661cm^{-1} are combined functional groups with transminttance under 60%T. At 3109 cm $^{-1}$ and 3319 cm $^{-1}$ WE find two functional groups with transmittance 74 %T and 68 %T respectively.
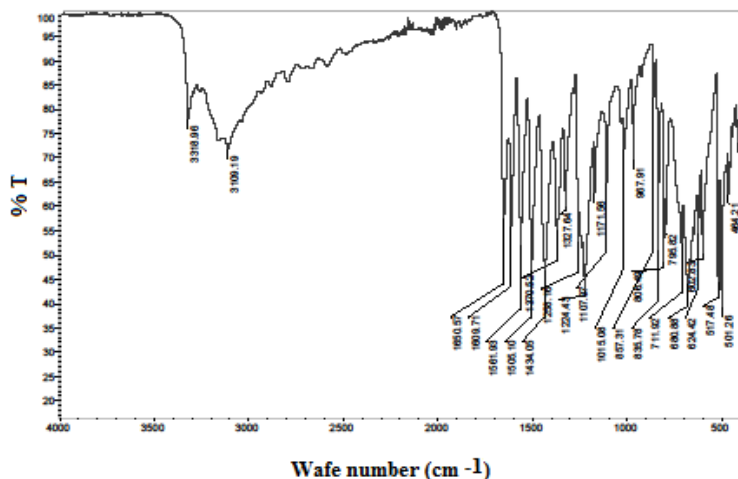

Fig.6. The IR spectrum of paracetamol

IR spectrum of nimesulide

The infrared spectrum of nimesulide is shown in Fig. 7. The main wave numbers obtained in the infrared spectrum and their corresponding assignment (bond, type and combined functional group) were characteristic of nimesulide.

The range of wave numbers 400-1600 cm^{-1} is a group of functions combined with transmittance below 70% T. At 3277.2 there is a functional grouping with 77% T.

IR spectrum of diclofenac sodium

The infrared spectrum of diclofenac sodium is shown in Fig. 8. The main wave numbers obtained in the infrared spectrum and their corresponding assignment (bond, type and combined functional group) were characteristic for diclofenac sodium.
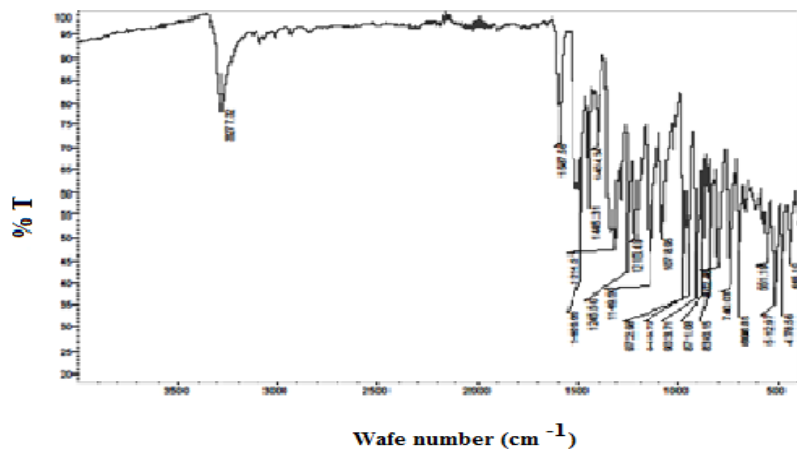
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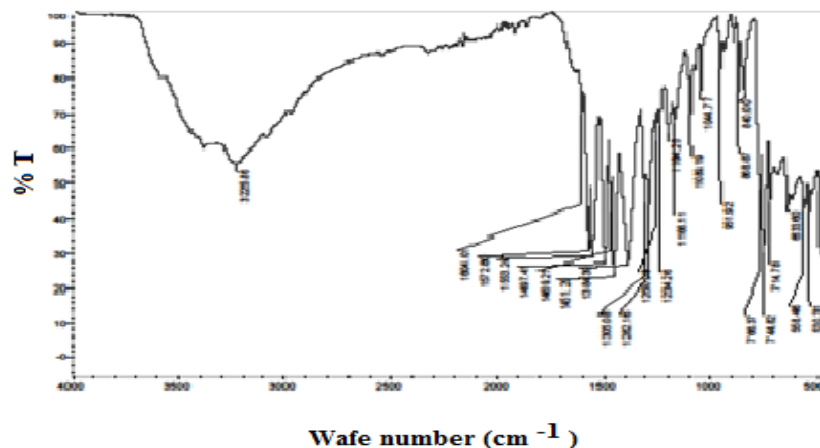Volume 5, Issue 1

Fig.7 IR spectrum of nimesulide

Fig. 8 IR spectrum of diclofenac sodium

The range of wave numbers 890 cm-1 - 1804 cm -1 is a group of functions combined with transmittance below 45% T. At 3205 there is a functional grouping with 55% T

Conclusions

Pain is one of the most common symptoms that cause a patient to see a doctor. Pain is an important alarm system in the protection of the body. Medications aimed at reducing or suppressing pain and fighting fever.

Antipyretic analgesics reduce fever by acting on the thermoregulatory centers that is, they decrease their functional level by tending to return it to normal values.

The spectral method of analysis is one of the most widely used methods of quality control for obtaining data on the structure and chemical composition of medicinal substances.

Our study can contribute to a spectrum atlas that can be used in drug control.

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