Scripta Scientifica Pharmaceutica, 2022;9(2):24-27
DOI: 10.14748/ssp.v9i2.8384

ISSN 0582-3250 (Print)
ISSN 1314-6408 (Online)

ORIGINAL ARTICLES

IR AND UV-VIS SPECTROSCOPIC ANALYSIS OF A NEW COMPOUND: N-[1-(4-HYDROXYPHENYL) AMINOETHILYDEN]-4-[1-(3,5,5,8,8-PENTAMETHYL-6,7-DIHYDRONAPHTALEN-2-YL)-ETHENYL] PHENYLCARBOHYDRAZIDE

Nadya Agova, Ivelin Iliev, Svetlana Georgieva

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Medical University of Varna

ABSTRACT

INTRODUCTION: Hydrazones are compounds that can be considered as hydrogenated azo compounds or as derivatives of hydrazine (H2N-NH2) in the structure of which one hydrogen atom at each nitrogen is replaced by a hydrocarbon group. In this work, we discuss the possibilities for analysis of a newly synthesized hydrazone of the retinoid bexarotene with acetaminophen using infrared (IR) and ultraviolet-visible (UV-VIS) spectroscopy.

AIM: The purpose of this study is to perform Fourier-transfrom infrared (FTIR) and UV-VIS spectroscopic analysis of a newly synthesized hydrazone of bexarotene.

MATERIALS AND METHODS: A newly synthesized hydrazone derivative was obtained according to the basic scheme of synthesis of bexarotene analogs. Infrared spectra 500-4000 cm^{-1} were taken on a Bruker FTIR spectrometer using ATR—a plug with a Smart iTR adapter. Spectra in the range 190–325 nm were recorded using UV-VIS spectrophotometer T60 UV with UVWin Software 6.0.

RESULTS: After a detailed comparison of the data obtained in the IR analysis of the reagents and the newly obtained hydrazone, a similar position and intensity of the spectral bands are reported. However, there are displacements in spectral bands and significant differences corresponding to the structural changes that have occurred. Different values for the wavelength of maximum absorption were measured with a UV-VIS spectrophotometer for bexarotene, Paracetamol, and the newly synthesized compound.

CONCLUSION: In order to confirm the data obtained by FTIR and UV-VIS spectroscopy, a further reversed-phase high-performance liquid chromatography-ultraviolet (HPLC-UV) analysis of the new hydrazone derivative should be performed.

Keywords: *retinoids, hydrazones, acetaminophen, FTIR spectra, UV-VIS spectroscopic analysis*

Address for correspondence:
Nadya Agova
Faculty of Pharmacy
Medical University of Varna
84 Tzar Osvoboditel Blvd
9002 Varna
e-mail: nadya.agova@mu-varna.bg

Received: September 28, 2022
Accepted: December 16, 2022

INTRODUCTION

Interest is growing in the hydrazone class of compounds due to the many diverse biological and clinical effects they possess, such as anticonvulsant, antidepressant, analgesic, anti-inflammatory, antiplatelet, antimalarial, antimicrobial, antimycobacterial, anticancer, vasodilator, antiviral, anti-HIV, anthelmintic, antidiabetic, and trypanocidal activities (1).

In pharmaceutical practice, the synthesis of hydrazones is associated with the possibility to provide minimal toxicity and maximum effective therapy for a number of diseases. There is a persistent search and development of new effective biologically active hydrazones. A number of hydrazone derivatives have been reported to exert significant biological effects (2,3).

These azomethines (-NHN=CH-) or hydrazones are an important class of compounds for the development of new drugs. They are condensation products of hydrazides with different aldehydes and ketones. Therefore, they can be considered as bound to a ketone or an aldehyde in which the oxygen atom is replaced by an $–NNH_2$ group.

The -C=N- double bond in hydrazones is an important structural component in drug design. It acts as a ligand for metal complexes, organocatalysis, and the synthesis of organic compounds.

This is the reason for the constant search for new approaches for the synthesis of hydrazone derivatives of compounds with already established therapeutic effects.

Bexarotene is an antineoplastic drug commonly classified as a rexinoid due to its selective activity at retinoid X receptors (RXRs) (4). It can be used systemically in patients with cutaneous T-cell lymphoma, specifically when patients have extensive plaques and tumors (5). It can also be given topically in patients with less severe and localized diseases.

The drug acetaminophen, also known as paracetamol, is used for the treatment of mild to moderate pain and the reduction of fever. It is available as an over-the-counter drug in various dosage forms. Acetaminophen injection is indicated for the management of mild to moderate pain, the management of moderate to severe pain with adjunctive opioid analgesics, and the reduction of fever. Because of its low risk of causing allergic reactions, this drug can be administered in patients who are intolerant to salicylates and those with allergic tendencies, including bronchial asthmatics (6). Hence, it became one of the most popular and extensively used drugs in the world for the treatment of pain and fever, especially for children.

The good knowledge of paracetamol and its wide application, along with the high potential of hydrazones as a chemical class of compounds, directed our work to the synthesis and subsequent analysis of hydrazones of the antineoplastic drug bexarotene with paracetamol (7).

In the present study, we describe methods for qualitative analysis of a product, a hydrazone of bexarotene and paracetamol, synthesized by us.

AIM

The aim of this study is to qualitatively characterize the newly synthesized bexarotene derivate. To achieve this aim, we used two main methods for the qualitative characterization of substances, namely infrared (IR) and ultraviolet-visible (UV-VIS) spectroscopy.

This article discusses IR and UV-VIS spectroscopy methods for the analysis of a newly synthesized N-[1-(4-hydroxyphenyl) aminoethilyden]-4-[1-(3,5,5,8,8-pentamethyl-6,7-dihydronaphtalen-2-yl) ethenyl]phenylcarbo hydrazide, which is a product of the interaction between the hydrazone of the antineoplastic drug bexarotene and paracetamol.

MATERIALS AND METHODS

The newly synthesized hydrazone derivative was obtained according to the basic scheme of synthesis of bexarotene analogs.

For the purpose of this study, we synthesized a new hydrazone derivative of the retinoid bexarotene. The process contains 3 major steps—esterification of the carboxylic group, hydrazinolisis and substitution of ketone to the newly formed hydrazone group. The result of the synthesis depends on the ketone used. As a ketone, we used paracetamol for the synthesis of the new derivative of bexarotene, shown in Fig. 1.

For the purpose of our work IR and UV-VIS spectroscopy were used.

Infrared spectrophotometry allows the determination of the molecule structures of various organic (and inorganic) substances based on the absorption spectra of emission.

Ultraviolet-visible spectroscopy is a type of electromagnetic spectroscopy that examines the interaction between light and matter. Historically, this branch of science arose when light from the visible spectrum was used to study the structure of matter, but later the UV and IR ranges of the electromagnetic spectrum began to be applied. This allows for

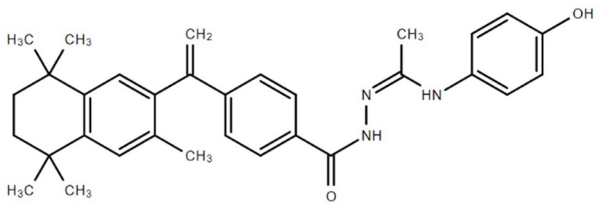

Fig. 1. Paracetamol was used for the synthesis of the new derivative of bexarotene

obtaining a significant amount of information about the structure of substances at an atomic and molecular level.

RESULTS AND DISCUSSION

ATR-FTIR analysis

To fully characterize the newly obtained structure, a comparative attenuated total reflection-Fourier-transform infrared (ATR-FTIR) analysis of the spectra of the starting compound—bexarotene, and the newly synthesized product was performed. Infrared spectra in the range 4000–500 cm^{-1} were recorded on a Bruker apparatus. The result of the FTIR analysis of the newly obtained after synthesis product is presented in Fig. 2.

After the synthesis, the newly obtained bexarotene derivative was dried and an FTIR analysis was performed.

The observed IR absorption in the spectra of bexarotene shows two main peaks of absorption at 1750–1700 cm^{-1} and 1450 cm^{-1} relating to the presence of the C=O and C-O bonds, respectively. Additional fundamental differences between the spectrum of bexarotene and the newly obtained molecule are taken into account more specifically in the observed displacement of the frequency of absorption inherent in the carbonyl group. It is reported that a variation in the frequency of absorption inherent in the presence of a carbonyl group was observed. This should be taken into account as structural changes affect the carbonyl group in the bexarotene molecule.

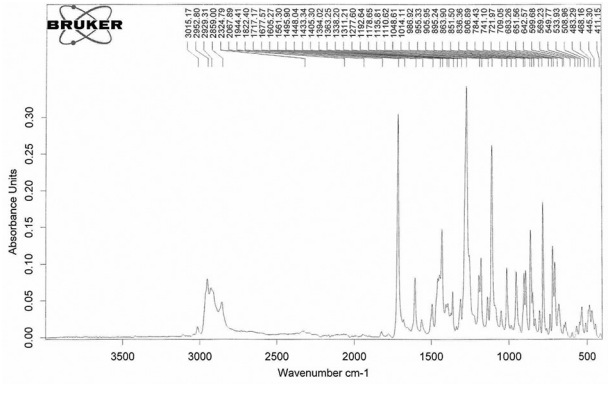

Fig. 2. The result of the FTIR analysis of the newly obtained after synthesis product

It is a possible result of the interaction with hydrazine and the formation of the target hydrazone. Bexarotene shows a typical C=O bond frequency at approximately 1690 cm^{-1}.

The FTIR spectrum of paracetamol was examined in detail, after which a comparison was made with the spectrum of the newly obtained hydrazone. The theoretical acetaminophen spectra also contained a peak at 3484 cm^{-1} that corresponds to an N-H stretch (7). This value was consistent with the literature absorption range of 3300 cm^{-1} to 3500 cm^{-1} which indicates an N-H bond of an amine functional group. The molecular structure of paracetamol comprises two main active groups, hydroxide (OH) and amide (N-C=O), attached to an aromatic ring. Characteristic vibration peaks recorded in the paracetamol spectrum were reported at 3325 cm^{-1} and 3162-3035 cm^{-1}. They are attributed to the stretching of the O-H and CH3 bonds.

Vibration peaks at 1653 and 1609 cm^{-1} are attributed to the C=O (amide I) and C=C elongations, respectively. In addition, maxima at 1555, 1506, and 1437 cm^{-1} refer to the presence of N-H, C-H, and C-C bonds, respectively.

Due to the close structural similarity, the IR spectra of the newly synthesized compound show similar bands with bexarotene and paracetamol. However, there are specific brands that are not observed in the bexarotene and paracetamol spectra.

UV-VIS spectrophotometric analysis

When UV light is absorbed by the molecules of a substance, electronic absorption spectra are observed: there is a transition (excitation) of the valence electron from the level of energy occupied by it to a higher energy level. Depending on the nature of the absorbed radiation, electron spectroscopy is often called UV and visible spectroscopy.

Ultraviolet-visible spectra were recorded using a UV-VIS spectrophotometer T60UV over a wavelength range of 190 to 325 nm on UVWin Software 6.0.

A solution for analysis was performed using 800 μg of newly sintered dry substance dissolved in 5 ml methanol (99.9%).

The wavelength of maximum absorption (λmax) of the newly synthesized molecule was at 202 nm, as shown in Fig. 3, with absorption of 0.616. Another peak was observed at 252 nm with absorption of 0.218 and a valley at 232 nm with absorption of 0.153. According to literature references bexarotene's λmax is at 264 nm. The recorded wavelength of maximum absorption of paracetamol in the same concentration and solvent was 243 nm. All spectrophotometric measurements were carried out in 1 cm matched quartz cells. The scan parameters used were low scan speed with an interval of 0.2 nm and spectral bandwidth of 2 nm.

The received results show that there is a difference in the wavelength of maximum absorption of the three analyzed compounds, because bexarotene and paracetamol served as reagents in the synthesis of the analyzed hydrazone. The differences we obtained in the analyses define the newly synthesized bexarotene derivative as a product of the synthesis.

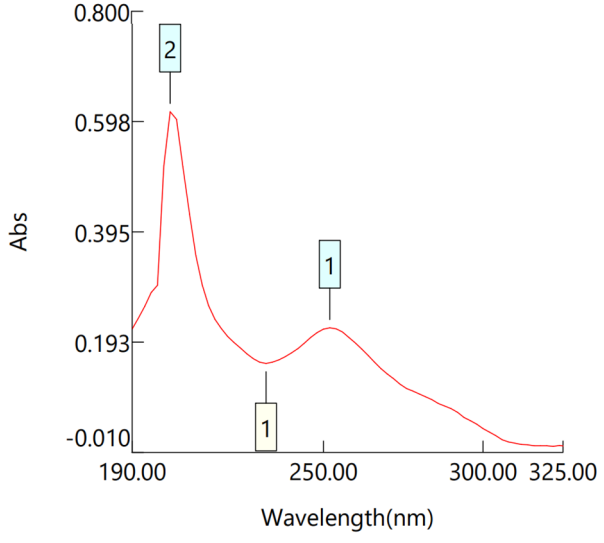

Fig. 3. The wavelength of maximum absorption (λmax) of the newly synthesized molecule.

CONCLUSION

After a detailed analysis of the data obtained during the IR analysis and UV-VIS spectroscopy, we can summarize that the obtained data correspond to the expected.

In the process of IR analysis, similar positions and intensities of the spectral bands are observed, similar to those reported for reagents. Nevertheless, there is displacement in spectral bands and considerable variation as a result of the accomplished structural changes.

In UV-VIS spectroscopy the recorded wavelength of maximum absorption for the three analytes (bexarotene, paracetamol, and the newly synthesized hydrazone) has shown different values. This differentiates the newly synthesized hydrazone from the other two molecules and thus it is more likely that the new molecule is indeed a hydrazone of the retinoid bexarotene with paracetamol.

In order to confirm the data obtained by FTIR and UV-VIS spectroscopy, a further reversed-phase high-performance liquid chromatography-ultraviolet (HPLC-UV) analysis of the new hydrazone derivative should be performed.

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