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FTIR and UV-Visible Spectrophotometric Derivatization Studies of Artemether

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Authors' contributions

This work was carried out in collaboration among all authors. Authors EEA, JAI and *ICU designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors JAI, EEA and CRC managed the analyses of the study. Authors EEA and JAI managed the literature searches. All authors read and approved the final manuscript.*

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ABSTRACT

This study was aimed at confirmation of the purity and identity of the artemether and development of an ultraviolet spectrophotometric method for the assaying of artemether utilizing p-nitroaniline as a derivatizing agent. Melting point and Fourier transform infrared spectrophotometer (FTIR) methods were used to confirm the purity and identity of the artemether used in the study. The derivatization process was carried out between 100 µg/ml of the artemether and 500 µg/ml of p-nitroaniline in different molarities (0.5, 1, 2, 3, 4, 5M) of HCl at 60ºC for 45 mins. The melting point ranged between 86-89ºC and the FTIR determination revealed a band at 3169.978 cm-1 due to O-H stretching vibration and C-H stretching at 2996.039 cm-1. There was no observed difference in wavelength between the p-nitroaniline spectrum and the spectra of the derivatized products in different molarities of HCl. p-nitroaniline may not be a proper derivatization reagent for the assay of artemether in pure or dosage form.

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1. INTRODUCTION

Malaria is a leading cause of morbidity and mortality in sub-Saharan Africa and thus has been a public health issue. To overcome the problem of malaria drug resistance (especially the one caused by *Plasmodium falciparium*), the use of artemisinin-based combination therapy (ACT) has been deployed for treatment of malaria across all ages. Artemether (semi-synthetic compound) is derived from artemisinin which is extracted from the Chinese herb sweet wormwood, *Artemisia* annua [1]. Artemether is the first-line therapy in the treatment of uncomplicated *Plasmodium falciparium* malaria. During the experiment, artemether does not show any significant absorption in the wavelength region of the UV-visible spectroscopy, since it lacks specific chemical groups (chromophoric) for reaction with a certain reagent to arise to coloured products [2]. Hence, derivatization has always been an option for assaying the artemether and its derivatives [3,4].

Analytical procedures for the assay of artemisinin-based drugs have been advanced for more than two decades, but there are challenges of numerous dilution processes, long reaction time and costly equipment [3,5]. Here, we reported confirmed the purity and identity of artemether and possible means for assay of artemether with the aid of a derivatizing agent.

2. METHODS

2.1 Reagent and Chemicals

Methanol, hydrochloric acid, distilled water, and *p*-nitroaniline (BDH, UK). Artemether was purchased from POCO Pharmaceuticals Limited, Nigeria. All other reagents and solvents were analytical grade.

2.2 Equipment

UV-visible spectrophotometer, Agilent technology (carry 60, England), Stuart (Smp 11, Germany), Bulk Scientific Fourier transform infrared Spectrophotometer model M350, Water bath (Adarsh An150 900l), Vortex mixer.

2.2.1 Determination of melting point

The melting point of the artemether was carried out using a standard procedure [6]. A 10-mg quantity of finely powdered drug sample was packed separately into a thin-walled capillary tube which had been sealed at one end. The capillary tubes and the thermometer were placed in appropriate apertures in the heating block. The temperature was raised uniformly at 10°C intervals and the melting point was determined.

2.3 Fourier Transform Infra-Red (FTIR) Analysis

A 2-g quantity of the artemether pure sample was triturated in a Buck 530 IR mortar with 0.5 g of KBr for effective release of bonds. Thereafter, 2 ml of nujol was introduced to form a paste before introducing it into the instrument sample mould. It was then scanned at wave number between 600 to 4000 cm^{-1} to obtain its spectrum.

2.3.1 Derivatization of artemether

The derivatization reaction was done using the methanol solutions of artemether and *p*-nitroaniline in different molarity of the acid media of HCl (0.5, 1, 2, 3, 4, 5M) at 60ºC for 45 min. Stock solutions of artemether (100 µg/ml) and *p*-nitroaniline (500 µg/ml) were utilized for the derivatization reaction. The UV-visible spectrophotometer was used for scan between 200-800 nm and methanol was used as blank [3].

2.3.2 Determination of lambda max of *p*-nitroaniline

p-nitroaniline (500 µg/ml) was pipetted into a test tube and 0.2 ml of 1M HCl was also added to the same test tube. The UV-visible spectrophotometer was used for a scan between 200 -800 nm and methanol was used as blank.

3. RESULTS AND DISCUSSION

The pure artemether sample was subjected to melting point determination. The melting point determination result was similar to the melting point established in the International Pharmacopoeia (IP) [7]. The melting point of pure artemether used in the study is within the range of 86-89ºC. The pure sample used for the study was of the same standard for the reference sample. This result confirmed the identity and purity of the artemether used in this

study. Pharmaceutical impurities are of public interest. Thus, impurities not been considered, have taken an unprecedented number of lives and touches all walks of life. Purity is a key parameter of the true chemical constitution of a substance and an essential physicochemical parameter in the formulation [8].

The FTIR of the artemether pure drug sample (Fig. 1) occurred at 3169.978 cm^{-1} due to O-H stretching vibration, C-H stretching at 2996.039 cm^{-1}, C-H bending at 1240.82 cm^{-1}, C-O bending at 1240.82 cm^{-1}, C-O-O-C bending vibration at 1328.226 cm^{-1}, O-O-C stretching at 851.914 cm^{-1}, and O-O stretching at 729.0468 cm^{-1} respectively. These values are comparable to those earlier reported [9,10].

The derivatization solution of artemether and p-nitroaniline gave an intense yellow colour in all acid media. The basic characteristics of derivatized products are the increase in spectral resolution, elimination of the influence of baseline shift and matrix interferences, and enhancement of the detectability of minor spectral features [11,12]. Derivative spectra are always sharper, better, and has a higher wavelength than the compound's pure form or nature [13].

The wavelength of *p*-nitroaniline in methanol is 370 nm. Uv-vis absorption spectra of molecules are highly dependent on the polarity of the used solvent. The polarity of the solvent has a great influence on the intensity, shapes, and position of the absorption bands. This is because with changing the polarity of the medium, the intermolecular interactions of the chromophore are changed which leads to the change of the energy difference between the ground state and the excited state. This solvent effect on spectra of the compound, resulting in a hypsochromic (or blue) shift with increasing the solvent polarity is usually called negative solvatochromism [14]. *P*-nitroaniline in the presence of methanol and HCl gave a wavelength of 371.9 nm (Fig. 2). The derivatized products gave 369.8 nm in 0.5M HCl, 371.3 nm in 1M HCl, 372.3 nm in 2M HCl, 372.4 nm in 3M HCl, 373.3 nm in 4M HCl, and 373.9 nm in 5M HCl (Figs. 3-8). The increase in the wavelength was observed as the molarity of the acid used increased. There is no difference in wavelength between the *p*-nitroaniline and the wavelength of the derivatized products in different molarity of HCl. These considerations indicate that the derivatization was unsuccessful and also *p*-nitroaniline may not be a proper derivatization reagent for assaying of artemether.

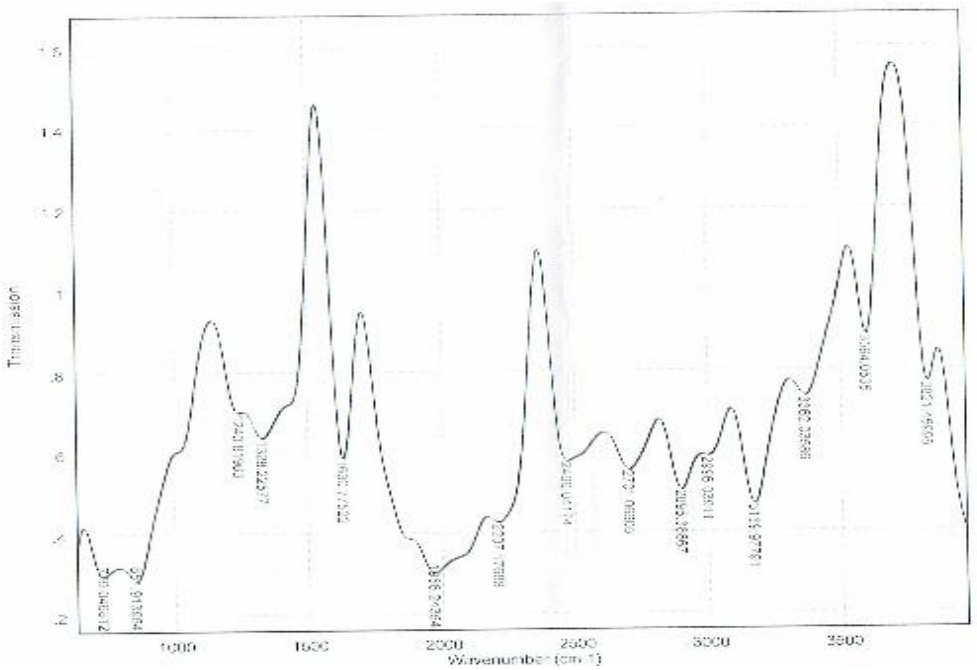

Fig. 1. FTIR spectrum of artemether

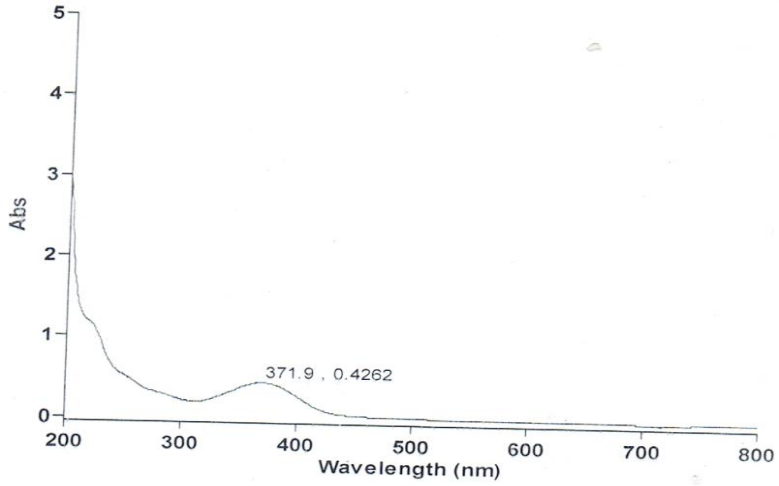

Fig. 2. Wavelength of *p*-nitroaniline in methanol and HCl

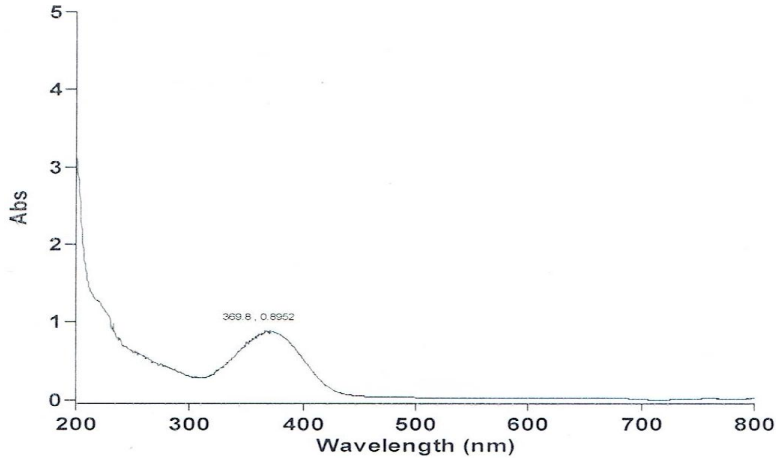

Fig. 3. Wavelength of artemether in methanol and 0.5M HCl

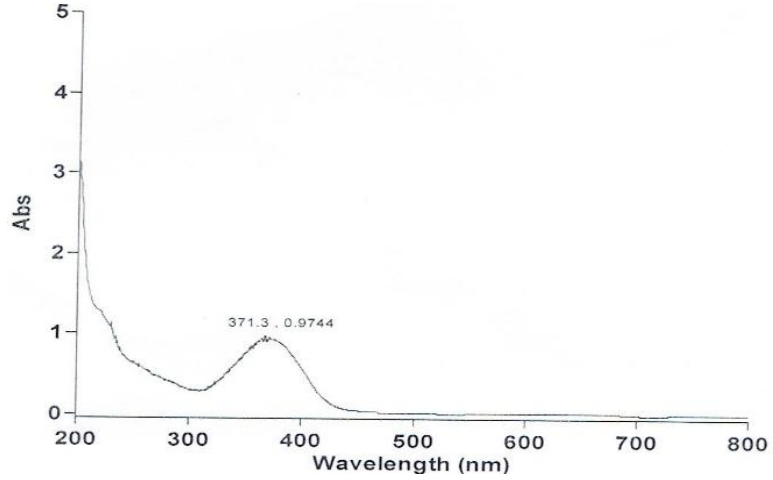

Fig. 4. Wavelength of artemether in methanol and 1M HCl

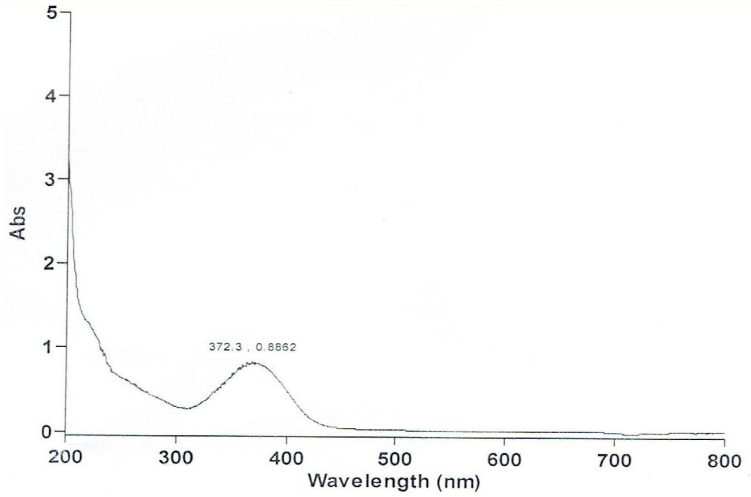

Fig. 5. Wavelength of artemether in methanol and 2M HCl

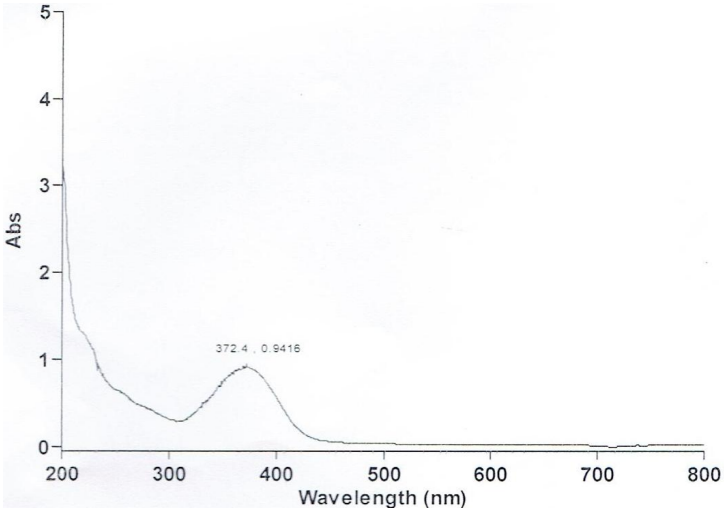

Fig. 6. Wavelength of artemether in methanol and 3M HCl

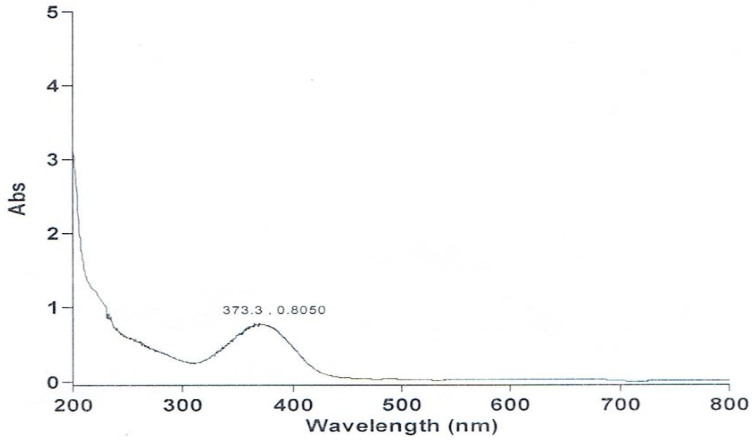

Fig. 7. Wavelength of artemether in methanol and 4M HCl

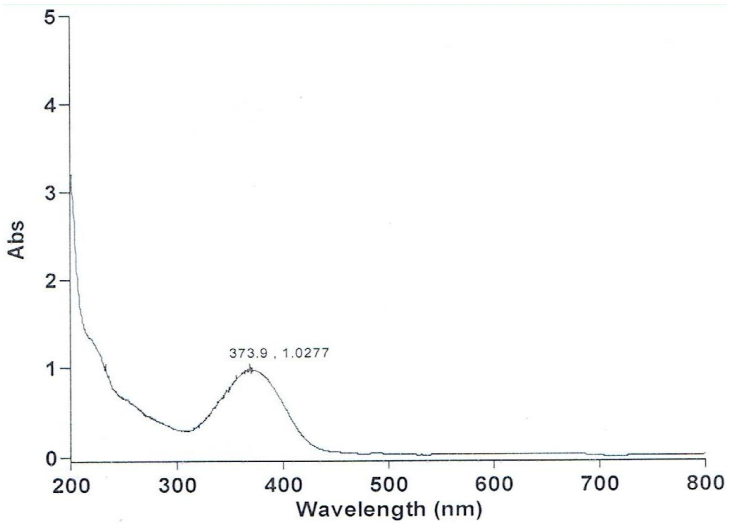

Fig. 8. Wavelength of artemether in methanol and 5M HCl

4. CONCLUSION

The melting point and IR analysis carried out confirmed the purity and identity of the artemether. Despite the variety and increase in molarity of the acid used in this study, yet the derivatization process was unsuccessful. These results suggest that *p*-nitroaniline may not be an ideal derivatizing reagent for the assay of artemether either in pure or dosage form.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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