Electronic and Fourier Transform Infrared Spectroscopic Characterization of Dicomponent Antimalarial drugs sold in Nigeria Drug Stores

I.E. Otuokere¹, C.O. Alisa² and C.O. Jonah¹
¹Department of Chemistry, Michael Okpara University of Agriculture, Umudike, Nigeria
²Department of Industrial Chemistry, Federal University of Technology Owerri, Nigeria.
*Corresponding Author E-mail: tosmanbaba@yahoo.com

ABSTRACT:
Dicomponent antimalarial drugs were purchased from different drug stores in Nigeria. The electronic and vibrational spectra characterization of these drugs was carried out. The electronic spectra of these drugs showed that they absorbed in the ultraviolet and visible region. The presence of chromophores C=C, C=N, S=O were suggested. The functional groups present in the infrared spectra showed that the active ingredients in the drugs were actually present. The suggested active ingredients of the dicomponent drug mixtures are sulfadoxine/pyrimethamine and dihydroartemisinin and piperaquine phosphate. Our forensic results showed that the antimalarial drugs are of quality standard.

KEYWORDS: Antimalarial, spectra, substandard, dicomponent, infrared, uv-visible

INTRODUCTION:
Malaria is considered to be the most prevalent vector-borne disease worldwide and is currently endemic in 97 countries [1]. Despite being preventable and treatable, malaria continues to be a life-threatening disease resulting in high levels of morbidity and mortality. Malaria is estimated to cause between 660,000 and over a million deaths every year and in 2012 there were an estimated 207 million cases of malaria [2]. Worldwide estimated malaria mortality rates between 2000 and 2012 fell by 42% across all age groups and by 48% amongst children under five years old [3]. However, the pace of this decrease slowed between 2011 and 2012 [3].

Africa is now at a critical stage in the struggle against a disease that saps its development. Without intervention, the crisis will deepen. But if national and global commitment and support for the Roll Back Malaria initiative can be put into action on the ground, then the devastation being wrought by malaria can be reversed [4]. Artemisinin combination therapy (ACT) is now the treatment of choice for uncomplicated Plasmodium falciparum malaria [5, 6]. Malaria endemic countries have switched to artemisinin-based combination therapy (ACT) for the treatment of acute, uncomplicated Plasmodium falciparum malaria [7]. The fixed dose combinations (FDCs) are strongly recommended over the blister packs to reduce the potential use of monotherapy [8]. FDCs are preferred to loose tablets because fewer tablets are involved and patient adherence can be improved [9]. Accordingly, all ACTs, except artesunate + sulphadoxine-pyrimethamine have been developed as FDCs. Since the efficacy of the ACT is partly dependent on the efficacy of its partner drug, there is a need to develop multiple ACTs. In Africa such as artemether- lumefantrine [10], artesunate-amodiaquine [11], pyronaridine-artesunate [12], dihydroartemisinin - piperaquine [13]. Poor-quality antimalarials have been a severe under-recognised public health problem, reducing the effectiveness of these drugs and threatening current treatment policies. There are three main types of poor-quality medicines; degraded, substandard and counterfeit. The WHO defines counterfeit drugs as those...
that are ‘deliberately and fraudulently mislabeled with respect to identity and/or source’, and may include those with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging [14]. Substandard drugs are produced with inadequate attention to good manufacturing practices and may have contents and/or dissolution times outside accepted limits, due to poor quality control [15]. In addition, degraded formulations may result from exposure of good-quality medicines to light, heat and humidity [16]. There is an increasing concern that a major impediment to malaria control is the poor quality of antimalarial medicines. Counterfeiting is one of the oldest and most profitable occupations [17]. However, even today, it remains difficult to detect, investigate or quantify. The World Health Organization (WHO) estimated that nearly half of the global pharmaceutical market is occupied by counterfeit drugs [18]. Recent estimates suggest that nearly 800 fake drug types [19] are within the legitimate pharmaceutical market structure, and globally there is a massive increase in counterfeit or falsified drug sales to over US$75 billion in 2010, an increase of more than 92% from 2005 [20]. Poverty, weak economies, poor regulatory systems, short supply, and the rising cost of therapeutic agents have created a corresponding increase in production of fake drugs because of the huge profit margin [21]. Both substandard and counterfeit drugs are serious problems, and remain as one of the most neglected public health issues [22], where counterfeiting is mounting to more than 60% in Third World countries [23]. WHO estimates about 60% of purchased counterfeited products did not have any active pharmaceutical ingredient (API), 17% contain too much or too little API, whilst another 16% contain the wrong ingredients altogether [24]. In this research, we report the electronic and Fourier transform infrared spectroscopic characterization of dicomponent antimalarial drugs sold in Nigeria drug stores.

MATERIALS AND METHODS:
Different brands of dicomponent antimalarial drugs were purchased from different Nigerian drug stores. There inscriptions were removed and they were labeled A, B, C and D respectively. The UV-visible spectra of the antimalarial drugs in solution were scanned between 200 – 800 nm on a Perkin Elmer model spectrum BX using chloroform as solvent. The Infrared spectra of the antimalarial drugs were carried out using FT-IR spectrometer by Perkin Elmer (Model Spectrum BX) equipped with caesium widow (4000-350cm\(^{-1}\)) in KBr pellets. Interpretations of the spectra were made.

RESULTS:
The electronic and Fourier transform infrared spectra of the malarial drugs (labeled A, B, C, D) are presented in Figures 1-8 respectively.
DISCUSSION:
In the electronic spectrum (Figure 1), the electronic absorption band at 192.63 nm has been assigned $\sigma \rightarrow \sigma^*$ transitions since this transition occurred in the vacuum ultraviolet region < 200 nm. The absorption bands 222.38, 281.02 and 318.65 nm were assigned $\pi \rightarrow \pi^*$, since these transitions occurred in the ultraviolet region. The suggested chromophores are C=C, C=N and S=O. In the FTIR spectrum of sample A, (Figure 2), the vibration frequencies 1155.24 and 1313.12 cm$^{-1}$ have been assigned $\nu$(S=O). The frequencies 3456.58, 3381.78 have been attributed to $\nu$(N-H) stretch. The vibration frequency 1081.94 cm$^{-1}$ have been attributed to $\nu$(R-O-R) functionality. 833.29 cm$^{-1}$ frequency has been assigned to $\nu$(R-Cl), 1595.29 cm$^{-1}$ was attributed to $\nu$(C=C) ring stretch. Aliphatic C-H stretch was found at 2952.38 cm$^{-1}$ in the spectrum.

The electronic spectrum of Sample B (Figure 3) showed absorption at 199.94 nm. This absorption was assigned $\sigma \rightarrow \sigma^*$ transitions because it occurred in the vacuum region < 200 nm. The bands 206.70, 232.80, 287.83 and 306.93 nm were assigned $\pi \rightarrow \pi^*$ transitions. The possible chromophores in the antimalarial drug that showed these absorptions are C=C, C=N and S=O. In the vibrational frequency of the FTIR spectrum of sample B (Figure 4), 1152.44 and 1314.65 cm$^{-1}$ were attributed to $\nu$(S=O). 3214.41, 3462.18 and 3372.76 cm$^{-1}$ wavenumbers have been assigned $\nu$(N-H) stretch. R-O-R, R-Cl, ArC=C and aliphatic C-H stretch functional groups were found at 1080.92 cm$^{-1}$, 836.04 cm$^{-1}$, 1591.46 cm$^{-1}$ and 2946.30 cm$^{-1}$ respectively.

The absorption band 205.75, 219.76 228.51, 244.26 and 320.40 nm which are in the ultraviolet region (Figure 5) were assigned $\pi \rightarrow \pi^*$ transitions. The absorption band at 484.06 nm appeared in the visible region. This band was assigned $\pi \rightarrow \pi^*$. The suggested chromophores in the antimalarial drug for these electronic transitions are C=C and C=N. The $\nu$(OH), $\nu$(R-O-R), $\nu$(aliphatic C-H), $\nu$(C=N), $\nu$(C-Cl) and $\nu$(C=N) functionalities appeared at 3350.14, 1037.76, 2929.97, 1644.75, 685.51 and 1037.76 cm$^{-1}$ respectively (Figure 6).

The electronic absorption bands 200.89, 207.99, 244.84, 256.55 and 272.54, 300.58, 330.73, 337.60 and 350.41 nm is present in the electronic spectrum shown in Figure 7. The possible chromophores in the test drug that might exhibit these bands C=C and C=N functional groups. These absorption have been assigned $\pi \rightarrow \pi^*$ transitions. The vibrational frequencies in the FTIR of sample D (Figure 8) showed 3434.00, 1017.79, 2931.24,
615.38, 1017.79, 3064.42 and 1126.76 cm\(^{-1}\) absorptions. These bands have been assigned \(\nu(\text{OH})\), \(\nu(\text{R-O-R})\), \(\nu(\text{aliphatic C-H})\), \(\nu(\text{C-Cl})\) and \(\nu(\text{C-N})\), \(\nu(\text{Ar-C-H})\) and \(\nu(\text{P=O})\) functional groups respectively.

Based on the electronic and Fourier transform infrared spectra, the following structures (Figures 9 and 10) have been suggested for the dicomponent antimalarial drugs.

**Figure 9:** Sulfadoxine-pyrimethamine dicomponent antimalarial drug

**Figure 10:** Dihydroartemisinin and piperaquine phosphate dicomponent antimalarial drug

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