Near-Infrared (NIR) Monitoring of H₂O₂ Vapor Concentration During Vapor Hydrogen Peroxide (VHP) Sterilisation

S. Corveleyn,1 G. M. R. Vandenbossche,2 and J. P. Remon1,3

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Purpose. There is an increasing use in the pharmaceutical industry of barrier systems such as transfer isolators, sterilisation tunnels and work station isolators. As Vapor Hydrogen Peroxide (VHP) sterilisation of isolators and lyophilizers becomes an important sterilisation method, there is an acute need for a VHP monitoring system to be used for in-process control and validation. In this study, near infrared (NIR) spectrophotometry was evaluated as a potential technique to monitor hydrogen peroxide. Additionally the H₂O₂ vapor permeability of different packaging materials, commonly used in steam and ethylene oxide sterilisation, was evaluated.

Methods. NIR spectrophotometry, using a gas cell connected with optic fibres, was evaluated as a potential technique to monitor hydrogen peroxide vapor and water vapor during VHP sterilisation of an isolator. A NIR spectrum was taken every 30 s during VHP sterilisation of an isolator. The influence of injection rate, air flow rate, working temperature and gas distribution was investigated. The H₂O₂ vapor permeability of different packaging materials was determined by placing the gas cell in the sterilisation bags and sealing the bags hermetically. The sterilisation bag was then subjected to VHP sterilisation.

Results. The NIR spectra taken at steady state sterilization conditions showed 4 absorption peaks: at 1364, 1378 and 1400 nm attributed to water and at 1420 nm attributed to H₂O₂ vapor. By measuring the absorbance level at these wavelengths, the actual concentration of H₂O₂ and H₂O vapor in the isolator was calculated. The water vapor permeation of the sterilisation bags, measured with NIR, appeared to be equal for all materials tested. Whereas Tyvek® was the most permeable material for hydrogen peroxide vapor (82.7% of the reference concentration outside the bag), only 30% was found in bags made of medical paper. Sterilisation bags consisting of laminate films and PVC sealed to medical paper showed intermediate permeability.

Conclusions. Near-infrared (NIR) spectroscopy using a gas cell with optic fibres is a useful technique to monitor VHP sterilisation cycles. There was a difference in H₂O₂ vapor permeability of different packaging materials, commonly used in steam and ethylene oxide sterilisation.

Key Words: hydrogen peroxide monitoring; near-infrared; VHP sterilisation.

INTRODUCTION

There is an increasing use in the pharmaceutical industry of barrier systems such as transfer isolators, sterilisation tunnels and work station isolators. These isolators are designed to be used for sterility testing, for batch and continuous production and to perform aseptic manipulations (1). The methods used to sterilize the interior of these isolators have to be effective and minimize or eliminate toxic residue concerns or materials compatibility problems. Vapor hydrogen peroxide (VHP) is a cold gas sterilant (2), which is a good alternative for previously used decontamination methods, such as ethylene oxide, formaldehyde and peracetic acid (3). Hydrogen peroxide vapor sterilisation has shown to be an effective biodecontamination method for a wide range of microorganisms (4). Previous studies revealed Bacillus stearothermophilus as the most resistant organism to VHP (5). Vaporised hydrogen peroxide (VHP) can be used in the biodecontamination of isolators (6,7) and lyophilizers (8). As VHP sterilisation of isolators becomes an important sterilisation method, there is an acute need for a VHP gas monitoring system that can be used for both in-process control and validation. In this study a near-infrared (NIR) spectrophotometer using a gas cell connected with optic fibres was evaluated as a potential technique to monitor hydrogen peroxide vapor and water vapor during VHP sterilisation. The H₂O₂ vapor permeability of different packaging materials, commonly used in steam or ethylene oxide sterilisation was evaluated.

MATERIALS AND METHODS

Hydrogen Peroxide Solution

The H₂O₂ solution used during sterilisation theoretically contained 31% (w/w) H₂O₂ (lotPE074C) and was obtained from Amso (Apex, NC, USA).

Sterilisation Cycles

A VHP 1001 Generator (Amso, Apex, NC, USA) was used to deliver hydrogen peroxide vapor to a 1.024 m² flexible wall work isolator Model 2003 and a 0.51 m² transfer isolator manufactured by La Calhène (Velizy Cedex, France) in a closed loop configuration. The VHP inlet port was positioned between the isolator blower and the HEPA filter. The sterilant gas was blown through the HEPA filter into the transfer isolator. The peroxide vapor outlet was directed through another HEPA filter. During all the experiments, the isolators were in a not loaded configuration. The programmed VHP sterilisation cycles consisted of three major steps:

1. Dehumidification: the isolator was dehumidified to 10.0% RH (relative humidity) to remove water vapor in order to prevent hydrogen peroxide vapor condensation. The minimum programmed dehumidification time was 10 min at 34 m³/h.
2. Sterilisation: the generator was programmed to deliver different amounts (1–3 g/min) of the hydrogen peroxide solution per minute and the air flow was varied between 17 and 34 m³/h. The total sterilisation time was kept constant at 30 min.
3. Aeration: after sterilisation, the isolator was aerated for 60 min at different air flow rates ranging from 17 m³/h to 34 m³/h.

An overview of all the sterilisation parameters during the experiments is given in Table I. Fans were used in this study to improve gas distribution (Etri, model 125 XR). In the transfer isolator a fan was located at the centre of the isolator floor and in the work isolator the 3 fans were located at 3 different sites:
Packaging Materials

The following packaging materials were used: two different medical paper sterilisation bags were used in this study: SBW medical paper (Griffith microscience, Herentals, Belgium) and SPS medical paper (SPS Laboratoires, Coulommiers, France); spunbonded polyethylene Tyvek® L1073B (Dupont, Luxembourg) and sterilizable RFS® bags, Tyvek L1073B sealed to a high density polyethylene film (Helvoet Pharma, Alken, Belgium); Teijin T85393, woven Tafeta 1/1 (Countdown, Wilrijk, Belgium); SPS Pealpack®, a polyester-polypropylene film sealed to a medical paper backing (SPS Laboratoires, Coulommiers, France); View-pac, a transparant blue laminating of polyester and polypropylene film, sealed to a paper backing (SBW, LMG Smith Brothers, Whitehaven, UK); sterilisation bags of polyethylene-polyamide laminate sealed to medical paper and boxes of PVC sealed to a paper back (Sterima, Bissegem, Belgium). The H₂O₂ vapor measuring cell was placed in the sterilisation bags and the bags were sealed hermetically, next the packaging material was subjected to sterilisation as described previously.

RESULTS AND DISCUSSION

Evaluation of the NIR Technique to Monitor VHP Sterilisation

Near-infrared (NIR) spectroscopy has been extensively used in the food industry for the past twenty years (9) and became an important technique in the pharmaceutical industry in recent years (10). NIR spectroscopy has been reported as a technique to determine the water content of freeze-dried products (11), and a rapid method for the identification of active components in tablets (12) and liquid formulations (13). NIR spectroscopy has also been evaluated as a potential monitoring system in the film coating process (14). NIR spectroscopy can be used to monitor VHP sterilisation, since the two major gas components, hydrogen peroxide vapor and water vapor, absorb NIR light at different wavelengths.

NIR spectra taken during different phases of the sterilisation cycle of a transfer isolator are shown in Fig 1. Spectrum A, taken at steady state sterilisation conditions, shows 4 absorption peaks in the NIR region. The peaks at 1364 nm, 1378 nm and 1400 nm, respectively are to be attributed to water. The absorption peak at 1420 nm is assigned to H₂O₂. The water vapor content of the isolator is determined by measuring the absorbance at 1364 nm, 1378 nm and 1400 nm. By measuring the absorbance at 1420 nm, the actual concentration of H₂O₂ vapor in the isolator was determined. Spectra B and C were taken during the aeration phase after 10 and 20 min, respectively. The absorption at 1364 nm, 1378 nm and 1400 nm, attributed to the water vapor decreased faster compared to the H₂O₂ vapor absorption. H₂O₂ vapor concentration was also monitored during sterilisation of the transfer isolator at different H₂O₂ injection rates (1.5, 1.8 and 2.5 g/min) and at a constant air flow rate of 22 m³/h. The theoretical H₂O₂ concentrations inside the isolator during these sterilisation cycles were calculated according to the method described by Amsco (15). The correlation between the NIR measured concentrations and the calculated concentrations is seen in Table II. There was a linear correlation between theoretical concentration and the actual concentration measured with NIR.