Abstract

To halt the pandemic of tuberculosis we need a rapid non-invasive screening tool to diagnose Tuberculosis. In search of a rapid point-of-care diagnostic tool for the diagnosis of pulmonary tuberculosis, we hypothesized that the unique signature of the exhaled chemicals of pulmonary tuberculosis cases can be identified with high accuracy by a novel colorimetric sensor array by total breath analysis.

Using porphyrin based sensor plates comprising of 24 indigenously synthesized coded porphyrin elements, a single breath test was done on 94 participants, 64 pulmonary tuberculosis patients (case) and 30 healthy volunteers (control). Significant differences in Red, Green and Blue (RGB) values of the porphyrin sensor elements were observed between pre and post exposure sensor array.

In overall impression from combined data, to differentiate pulmonary tuberculosis (P-TB) cases from healthy controls by our sensor array, we could reach up to sensitivity of 85.42 percent (ICh), specificity up to 78.89 percent (ICa) and positive predictive value up to 86.23 percent (ICa). Overall, analyte ICa consistently showed highest specificity and positive predictive values (≥74%) in phase-1, phase 2, and compiled data of both first and second phases. Conclusive level (>10) of Likelihood ratio positive value (LR+) could not be reached by our compounds with ICa exhibiting a value of 2.94 followed by ICd which shows a value of 2.24, both of which falls in the category of “Small increase in the likelihood of disease”.


In the overall analysis of the binary logistic regression, 4 (four) analytes viz. ICa, IIBa, ICd, ICe were fairly strong components by showing high statistically significant reaction (p<0.001). The sensor elements that shows statistically significant reaction (p<0.05) are I, IAb, IEc, ICc, ID, IAe, ICg, IB, ICh and IAb1. Out of 24 porphyrin used in the present research work 14 of them emerge as statistically significant with 95% confidence which is a good result when one considers the constraint present in the present investigation.

Overall, ICa emerges as the best sensor element amongst the 24 porphyrin derivatives used in the present investigation.

The most important findings of the study are that a particular class of porphyrin and its derivatives are better sensor than other class of porphyrin and its derivatives. Porphyrins substituted with electron withdrawing groups are better sensor elements and specifically one particular group was highly effective. We could identify specifically a porphyrin derivative which was more responsive towards healthy participants as compared to diseased persons.

In our study, porphyrin array-based chemical sensing showed promising results for the direct diagnosis of pulmonary tuberculosis. The quality of interaction with organic volatile compounds can be controlled by suitable changes in the porphyrin macrocycle like peripheral substituent and central metal. This would lead to fine tuning of sensor array by identifying responsive porphyrin derivatives with better predictive value and incorporation them in a single array for enhanced responses.
It would be worth evaluating colorimetric porphyrin elements based sensor array in more detail as a likely cost-effective futuristic model of non-invasive entrant in diagnostic algorithms to halt the pandemic of tuberculosis.

**Keywords:**

Porphyrin, Pulmonary Tuberculosis, Total Exhaled Breath, RGB analysis, Colorimetric sensor