Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 22 May 2026
Revised 29 June 2026
Accepted 12 July 2026

Natural Resources for Human Health 2026, Vol. 6 (7s): 801–807

KEYWORDS:
Saliva, disease detection, VOC, gas analysis

Human Disease Detection with Saliva Gas Analysis

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ABSTRACT: Saliva is a complex fluid containing hormones, antibodies, enzymes, microorganisms, and their metabolites, and cellular debris. Saliva analysis has conventionally been carried out for detecting various diseases by healthcare providers. Primarily it is used for detecting hereditary disorders, autoimmune diseases, infectious diseases and certain cancers. Saliva analysis thus serves as a powerful and versatile diagnostic tool for both local (oral) and systemic (whole body) disease detection and management.The gases evolving from saliva are indicative of human systematic health. Disease detection with saliva gas analysis is an emerging noninvasive technique used to investigate disease indicators in saliva through Volatile Organic Compound (VOC) analysis. Many of saliva VOCs gases evaporate easily at room temperature. The composition of these VOCs changes based on the body's physiological and pathological state. The VOCs in saliva originate from systemic blood circulation, oral micro biome, oral tissues and stomach. The metabolic change occurring due to diseases is reflected in the saliva VOC footprints. Therefore, this paper focuses on identification of disease from saliva gas analysis. The set of sensors comprising of conductivity, VOC, methane, oxygen and ammonia gas sensors is deployed for saliva gas capture. The experimental results are presented for disease detection by comparing the detected gas levels with thresholds.

1. INTRODUCTION

Disease detection using saliva gas analysis is an emerging and highly promising field that leverages the rich biomarker content and non-invasive accessibility of saliva for health diagnostics [1]. Saliva contains a variety of peptides, ions, metabolites and gases that reflect both oral and systemic health states, allowing researchers and clinicians to monitor, diagnose and predict disease progression without the discomfort of blood draws or invasive procedures [2]. Advancements in biosensor technology have played a crucial role, with new devices capable of analyzing specific gas-phase biomarkers in saliva providing rapid, real-time results and facilitating early detection of diseases and metabolic syndromes [3].

Saliva analysis offers several advantages over traditional diagnostic fluids, including ease of collection, reduced patient discomfort, and minimal requirements for specialized storage or handling [4]. The COVID-19 pandemic accelerated interest in saliva-based diagnostics, demonstrating their effectiveness in detecting a range of viral pathogens and encouraging broader acceptance of saliva for screening and surveillance [5]. Gas sensors and biosensors designed for saliva have reached high sensitivity and specificity, able to detect molecular changes associated with disease onset. These devices monitor VOCs, proteins, enzymes and other molecular signatures that can serve as early warning signals for various disorders [6].

Saliva has been recognized as a clinical biofluid rich in proteins and genomic markers; however the VOCs emitted from saliva are being under scrutiny. These gaseous molecules are metabolic by-products that diffuse from the systemic circulation into the salivary glands through the dense capillary beds. The gas above a saliva sample serves as a chemical fingerprint, reflecting the physiological and pathological state of the human body [7, 8]. The primary clinical appeal of saliva gas analysis leads to detect systemic diseases at early stages without the need for invasive blood draws. The specific VOC patterns are associated with metabolic activities, such as elevated acetone in diabetic patients and even the presence of distant malignancies like lung or

breast cancer. As the collection process is painless and requires minimal specialized training, it is particularly suited for pediatric and geriatric populations, as well as for longitudinal health monitoring in point-of-care settings [9].

From a technical perspective, the analysis of these gases involves sophisticated detection systems ranging from portable Electronic Noses (e-noses) [10]. These systems must distinguish between systemic biomarkers and those produced locally by the oral microbiome, such as volatile sulfur compounds associated with periodontitis. While challenges remain regarding the standardization of sample collection, the integration of intelligence is rapidly improving the sensitivity and specificity of these liquid biopsy gas profiles [11].

Recent research focuses on integrating advanced materials with saliva-based biosensors, enhancing disease detection capabilities and making these systems suitable for point-of-care and home-based monitoring. The evolution of machine learning and next-generation sequencing further expands the predictive power of saliva gas analysis, promising greater reliability and broader applications in personalized medicine.

2. MATERIALS AND METHODS

2.1 Saliva Gas Analysis

Saliva gas analysis for disease detection, especially through the identification of VOCs, has recently gained attention as a promising and non-invasive method for biomedical diagnostics. Saliva is recognized as an ideal biofluid for disease monitoring due to its accessibility, non-invasiveness and reflection of systemic physiological states. Diseases alter cellular metabolism, resulting in shifted VOC profiles detectable in saliva, which serve as potential biomarkers for a variety of conditions and diseases [12]. It facilitates the rapid, cost-effective and scalable screening of large populations, reducing reliance on invasive procedures. The salivary VOC profiling using GC-MS can distinguish OSCC patients from healthy controls with high diagnostic accuracy [13]. Notably, acids and ketones show significant elevation in cancer patients, correlating with disease progression and stages. Combined saliva and breath analysis (using biosensors) allows early detection of respiratory infections, including seasonal viruses and COVID-19. Saliva molecular tests provide sensitivity comparable to nasopharyngeal swabs [14].

Saliva contains metabolic waste products like urea and creatinine, which accumulate in the body as kidney function declines [15]. Studies have demonstrated a strong positive correlation between salivary and blood levels of these compounds, making them reliable indicators of kidney function [16]. Breath analysis offers another non-invasive avenue for chronic kidney disease detection by profiling VOCs, which are metabolic by-products influenced by impaired kidney function [17]. Kidney and liver dysfunction leads to raised ammonia (NH_3) levels due to impaired conversion of nitrogenous wastes [18, 19]. Elevated salivary ammonia may contribute to diagnosis in cases where blood ammonia levels are already considered important for hepatic encephalopathy and other metabolic disorders [20, 21].

Methane gas in saliva, produced by methanogenic bacteria, has been studied as a potential biomarker for certain gastrointestinal and metabolic diseases, especially those linked with microbial dysbiosis and small intestinal bacterial overgrowth [22]. Methane concentrations are measured in breath or saliva tests to help diagnose conditions that affect gut motility, microbiota, and metabolism. Patients with methane-predominant bacterial overgrowth are up to five times more likely to suffer from chronic constipation than those with hydrogen-predominant overgrowth [23].

Oxygen in saliva serves as indirect gas biomarker, plays a crucial role through its involvement in oxidative stress and antioxidant activity, which are strongly correlated with several oral and systemic diseases. The balance between reactive oxygen species (ROS) and antioxidant defences in saliva influences disease progression and oral health status [24]. Studies have found that antioxidant enzyme levels in saliva are significantly reduced in patients with chronic periodontitis and ischemic heart disease, reflecting increased oxidant stress and potential tissue damage. Measuring these oxygen-related oxidative stress markers in saliva offers valuable insights into both oral and systemic health [25].

2.2 Saliva Gas Parameters

The table 1 shows the saliva parameters for assessment of the disease.

Table 1: Saliva parameters and disease

Parameter	Disease
pH	Acidity, dental decay, oral health
Conductivity	Hydration, electrolyte balance, oral health, systematic disease (salt contents in body fluid)
Glucose	Diabetic
Gas	Gastrointestinal Disorders by Volatile Organic Compounds (VOCs) Inflammation and Infections by Nitric Oxide (NO) Respiration Carbon Dioxide (CO2) and Oxygen (O2) Liver disease by ammonia (NH3) Stomach health by methane (CH4) and hydrogen (H2)
Photometry	Glucose, kidney functioning

3. RESULTS AND DISCUSSION

The experimental setup for saliva gas analysis consists of gas sensors for measurement of oxygen, ammonia, methane and VOCs. The experimental setup is also equipped with a conductivity sensor. The photograph of experimental setup is shown in figure 1.

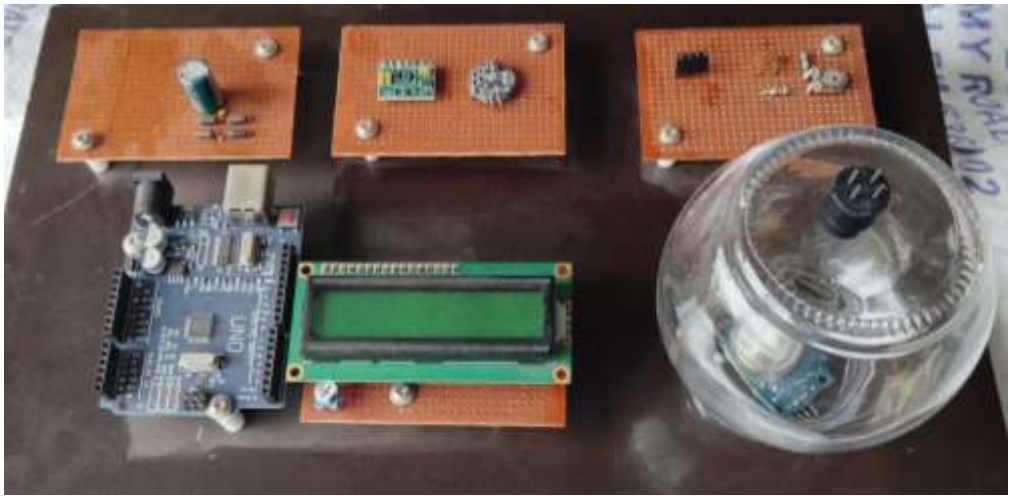

Figure 1: Experimental Setup

The details of sensors used for sensing the saliva gas, nominal range, illness range and disease type are mentioned in table 2. The illness range and nominal range re determined by noting the experimental values obtained from saliva samples. The dataset of these parameter measurement is made available in [26].

Table 2: Saliva Gas parameters sensors, normal range and illness range

Gas / Parameter	Sensor	Normal value range	Illness range	Disease Type
Reactive Oxygen	DF Robot SEN0465-ND	260 – 300	< 250	Oral decay
Methane	ZC05	0 – 10	> 10	Gastrointestinal disorder Liver functioning
Ammonia	MQ137	0 – 95	> 95	Kidney functioning Creatinine level
Conductivity	LFS1305	3400 – 3600	< 3400 & >3600	Digestion, Kidney disease if conductivity > 3600

The saliva sample is taken in the quantity of 2 to 3 ml. A part of collected sample (0.3 - 0.5 ml) is placed on conductivity sensor for measurement of saliva conductivity. The conductivity sensor assist in diagnosis of periodontal disease (dental health) and kidney functioning. The remaining quantity of saliva is taken into a watch glass and placed in inspection chamber. This sample spends a warm-up time of 15 minutes inside the inspection chamber. The inspection chamber is constructed in such a way that it does not allows the evaporated gases from saliva to escape. The evaporated gases from saliva are sensed by various gas sensors in the inspection chamber. The data of sensors is process through a controller board which is programmed to compare the incoming sensor data with threshold levels for diagnosis and disease detection. The observation results for various samples of saliva with disease detection are mentioned in table 3. The disease detection is also compared with pathological reports for validation. It is seen that the disease detection with saliva gas analysis closely matches pathological testing with blood test, urine test and stool test results for identifying the diseased organ.

Table 3: Disease detection from saliva gas analysis and comparison with lab report

ID No.	Conductivity (µS/cm)	Oxygen (ADC data)	Methane (ADC data)	Ammonia (ADC data)	Disease (Gas analysis)	Pathological Lab report	Diagnosis
S_01	3450	263	124	81	---	---	Healthy
S _02	3478	268	101	87	---	---	Healthy
S_03	3677	274	121	99	Kidney	Creatinine – 1.43	Urine infection
S_04	3490	278	118	81	---	---	Healthy
S_05	3392	230	259	117	Stomach	Stool test Bacteria positive Creatinine – 1.37	Loose motion (Gastro)
S_06	3352	265	131	102	Stomach	Stool test Bacteria positive Urine test: amber colour	Gastro
S_07	3512	268	153	86	Liver	Liver functioning test ALT – 69 AST - 59	Stomach ache
S_08	3524	264	201	81	Liver	Liver functioning test ALT – 67 AST – 56	Stomach ache
S_09	3465	235	157	118	Oral decay Kidney	Creatinine – 1.56	Urine infection (kidney stone)
S_10	3511	269	145	99	Stomach	Stool test Bacterial infection	Stomach ache
S_11	3462	262	123	82	---	---	Healthy

ID No.	Conductivity (µS/cm)	Oxygen (ADC data)	Methane (ADC data)	Ammonia (ADC data)	Disease (Gas analysis)	Pathological Lab report	Diagnosis
S_12	3472	266	121	98	Kidney	Creatinine – 1.44	Urine infection
S_13	3502	264	126	96	---	---	Healthy
S_14	3509	261	124	97	---	---	Healthy
S_15	3557	257	211	86	Liver	Liver functioning test ALT – 69 AST – 57	Stomach ache
S_16	3571	259	132	116	Kidney	Creatinine – 1.45	Urine infection
S_17	3516	254	124	117	Kidney	Creatinine – 1.46	Urine infection
S_18	3488	262	186	91	Liver	Liver functioning test ALT – 69 AST – 57	Stomach ache
S_19	3521	272	202	88	Liver	Liver functioning test ALT – 69 AST – 57	Stomach ache
S_20	3533	268	198	92	Liver	Liver functioning test ALT – 69 AST – 57	Stomach ache

4. CONCLUSION

This paper discusses disease detection with saliva gas analysis. The experimentation involves measurement of saliva conductivity and concentration of methane, ammonia and oxygen to diagnose the diseased organs, particularly, kidney, liver and stomach. The experimental setup of saliva gas analysis is able to detect the diseased organ within 20 minutes from obtaining the saliva sample. The pathology report confirms the detection of diseased organ. The diagnostic techniques with saliva gas analysis needs standardization and hence the future research needs to be directed towards validation and standardization processes.

ACKNOWLEDGEMENTS

The authors acknowledges the Department of Electronics and Telecommunication, AISSMS IOIT, Pune for extending their facilities during conduction of the research work

AUTHOR CONTRIBUTIONS

Vicky Nalawade: Conceptualization, Investigation, Methodology, Laboratory Analysis, Writing and Editing.

Vinayak K. Bairagi: Supervision, Writing, Review & Editing.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

Ethical approval was taken from patients while taking saliva samples for this study.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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