SWEAT ANALYSIS: A PAINLESS ALTERNATIVE TO REAL-TIME VITAL SIGNS ANALYSIS

PART 5: DISCUSSION OF CURRENT RESEARCH

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*Applications of Sweat Analysis*

The first major application of sweat analysis is in the area of disease diagnostics. In the last three decades, much emphasis has been laid on the use of sweat in diagnosing diseases. Cystic fibrosis provides the best example of a disease whose diagnosis depends on sweat analysis. The rationale for this choice is that the disorder arises due to transformations in the CFTR proteins, interfering with the formation and production of sweat, leading to high levels of chloride in sweat (Emaminejad *et al*., 2017). Therefore, the sodium to potassium ratio is an invaluable biomarker in the identification of cystic fibrosis. Dehydration is another problem that afflicts cystic fibrosis patients. As sweat analysis can also detect dehydration in patients, this procedure can help to confirm a diagnosis. Extensive research has been done to establish best practices in the use of sweat analysis to diagnose cystic fibrosis.

Currently, it has been established that two cystic fibrosis diagnoses are possible based on sweat chloride levels: typical and atypical (Farrell *et al*., 2017). When a patient presents with at least one physical symptom and lab tests yield chloride levels that exceed 60 mmol per litre of sweat, then a real positive diagnosis, also referred to as typical cystic fibrosis, is made. On the other hand, atypical cystic fibrosis is diagnosed when the sweat chloride levels range between 30 and 60 mmol per litre of sweat. These cut-off values have been established based on the normal range of sweat chloride in infants and in the elderly, which is 30 to 59 mmol/L and 40 to 59 mmol/L, respectively. Contemporary studies have also looked into sweat potassium as a prospective biomarker for the primary diagnosis of cystic fibrosis to inform treatment efforts

(Farrell *et al.*, 2017). Nonetheless, the clinical use of this alternative biomarker is still undergoing research.

Recent studies have also shown that sweat offers valuable biomarkers for the diagnosis of diabetes. Diabetic biomarkers in sweat include the mean change in sweat rate, sweat constituents and the relationship between glucose levels in sweat and blood (Oh *et al*., 2018). Comparing glucose levels in sweat and blood provides more reliable outcomes as long as no extraneous glucose is introduced into sweat samples. The most commonly used anatomical site for sweat glucose sampling is the foot. An uncomplicated indicator test that uses colour change is employed. The patch is expected to change from blue to pink within 10 minutes of the addition of 6 drops of water. This colour change is attributed to the conversion of anhydrous cobalt II chloride, which is in blue in colour, to the hydrated version of the salt that exhibits as pink.

For the detection of lung cancer, a sweat-based diagnostic procedure has been proposed. The assay distinguishes the metabolomics of healthy and sick individuals and involves the dilution of sweat samples with 0.1% formic acid. The mixture is then analysed using LC-TOF/MS, which requires only 10 microlitres of sweat (Jadoon *et al.*, 2015).

Sweat analysis can also be applied in drug testing, which is achieved via two methods: early and late testing (Jadoon *et al.*, 2015). Early testing entails the use of immunochromatographic approaches for the qualitative identification of drugs used within the last 24 hours. In comparison, late testing involves the patch technique for the qualitative identification of drugs used in the last 7 days. This method is commonly employed to follow up on previously identified drug users to confirm abstinence. Therefore, sweat comprises a suitable sample for doping control. The whole human body excretes an average of 300 to 700 millilitres of sweat per day. This volume can potentially contain a small but measurable proportion of drugs that are eliminated via paracellular and transcellular pathways in the skin (Jadoon *et al*., 2015). Examples of drugs that are known to be excreted through sweat in measurable levels include amphetamines, opiates, gamma hydroxybutyrates, buprenorphine, cannabinoids and cocaine. Moreover, the levels of ethanol produced in sweat over time can be determined.

*Novel Biomarkers in Sweat*

Another notable advance in sweat analysis is the use of genomics and proteomics to identify novel biomarkers in sweat. One such biomarker is dermcidin (DCD), a peptide made up of 47 amino acids. In elevated salt concentrations as well as over a wide pH range, this peptide demonstrates antimicrobial activity against various microbes. Therefore, sweat is thought to play a vital role in the populations of human skin microflora. It has also been observed that aggressive breast carcinomas express DCD and its receptors in significant quantities. Such features are also seen in cells that metastasise to lymph nodes and brain neurons. These observations indicate that DCD plays a vital role in tumorigenesis by encouraging the growth and persistence of cells that form breast carcinomas (Yu *et al*., 2017).

Prolactin inducible protein (PIP) is a new prognostic biomarker that is generated in some exocrine tissues such as sweat glands. PIP is also expressed excessively in breast and prostate malignancies that have metastasised to other organs (Kachman et al. 2018). Moreover, a study performed on healthy and schizophrenic patients has led to the identification of prognostic biomarkers in sweat. Eccrine sweat has numerous proteins and peptides compared to serum, which shows that eccrine sweat can provide unique disease-associated biomolecules.

*Hybrid Sensing Systems*

Imani *et al*. (2016) created a wearable hybrid sensing system that enables concurrent real-time checking of biochemical data in the form of lactate and an electrophysiological signal. This hybrid system facilitates more in-depth fitness monitoring as opposed to either sensor in isolation. The two sensing technologies consisted of modalities, an amperometric lactate sensor made of three electrodes and a bipolar electrocardiogram sensor, which were co-attached to a flexible material to be affixed to the skin. The instrument, authenticated on human subjects, demonstrated the ability to obtain physiochemical and electrophysiological data simultaneously with minimal interference. This work paved the way for the creation of an innovative group of hybrid sensing appliances.

Even with the creation of wearable sweat sensors, few gadgets can gauge biochemical data and biological indications at the same time, which has constrained combined data analysis and extensive medical use. Hong *et al*. (2018) developed a multifunctional wearable system that combined sweat-based sensing and monitoring of vital signs to quantify glucose levels before and after exercise. The system comprised a disposable glucose sensing strip that used sweat as the test fluid and a smart band. The combined system used a single control software that evaluated glucose concentrations in sweat and checked vital signs continuously. The vital signs recorded by the system included blood oxygen concentration, heart rate and physical activity. Hong *et al*. (2018) evaluated the efficacy of the system using human sweat samples collected from various anatomical sites as well as samples collected using different techniques in long- and short-term investigations. Consequently, the protocol was optimised for health surveillance. The blending of sweat glucose data and vital signs before and after exercise made it possible to determine blood glucose changes during physical activity. As a result, it was possible to acquire valuable data to help in precluding hypoglycaemic shock during intensive exercise. Furthermore, the amalgamated wearable system paved the way for the development of new, all-inclusive tailored health management strategies by merging the analysis of crucial metabolic and physiological health pointers.

*Novel Wearable Sweat Sensor Devices*

In most cases, patients often make contact with their medical providers after they have acquired diseases with pronounced symptoms. Thereafter, the patients become receivers of passive care and monitoring by health experts. This strategy is not helpful in the prevention of disease initiation because it places the emphasis on diagnostics and treatment instead of prevention and proactive health care. This approach also prevents individuals from taking charge of the monitoring of their health. The advancing field of wearables intends to address these shortcomings of consolidated, reactive health care by allowing individuals to have an insight into the functioning of their bodies. The longstanding foresight is to create sensors that can be integrated into wearable formats such as wristbands, clothes, patches or tattoos to investigate various body indicators continuously. Through the transmitting of physiological data as the body changes from a healthy to a diseased state, people will be capable of keeping track of their health in the absence of trained experts and costly equipment (Lee *et al.*, 2017). Recent advances in wearable sweat-sampling instruments have circumvented most of the conventional issues in sweat detection by enabling molecular-level discernment of the subtleties of human bodies.

Numerous wearable sweat sensors that have been developed recently blend varying form factors, substrates and identification mechanisms. To facilitate ongoing fitness checking, these sensors have been incorporated into everyday athletic fittings such as wristbands or headbands, which can be easily assumed without interfering with or hampering movement. Patch-style platforms are desirable for medical uses due to their ability to stick to the skin inconspicuously and because of their ease of application on various parts of the body. Furthermore, integrated iontophoresis capabilities can be incorporated to facilitate the extraction of equilibrium sweat from specific anatomical sites. Several substrates have been created to execute the various forms of sensors, for example, momentary tattoos, pliable polymers and fusion systems that merge malleable plastics with conventional silicon integrated circuits.

Different sensing instruments exist for the identification of analytes in sweat. Electrochemical detection is a widely used approach because of its adaptability. This technique quantifies electric currents or potentials at specific electrodes to determine the concentration of analytes. Colorimetric detection is another well-known method that depends on quantifiable colour changes following the exposure of specific reagents to the target analytes. Other schemes consist of impedance-centred and optical detection. Even though most of these methodologies have been used in the identification of non-complex ions and metabolites, they can still be modified or implemented alongside other technologies such as synthetic polymer models or affinity-based aptamers for discriminatory identification of multifaceted molecules. However, a need remains to examine the sturdiness of these techniques for on-body sensing.

Wang *et al*. (2018) developed a new kind of elastic and electrochemical sweat system made by putting copper submicron pieces on self-supporting graphene paper containing a single layer of $MoS_2$ nanocrystals. The system aimed at detecting glucose and lactate in biological samples. An amperometric i-t technique was used to quantify glucose and lactate. Glucose levels ranging from 5 and 1775 μM were detected, while the lactate levels ranged from 0.01 to 18.4 mM (Wang *et al*., 2018). In comparison, the limits of detection for glucose and lactate were 500 nM and 0.1 μM, in that order. The system exhibited a prompt response, acceptable selectivity, excellent reproducibility and exceptional adaptability, making it an ideal model for checking glucose and lactate levels in human sweat. The structural incorporation of a three-dimensional transition metal, zero-dimensional transition metal sulphide and two-dimensional graphene provided a novel intuition into the creation of bendable electrodes for the checking of sweat glucose and lactate as well as a broad range of uses in bioelectronics, biosensing and lab-on-a-chip contraptions. A similar study was done by Lee *et al*. (2017) with similar outcomes.

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