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A Narrative Review of Research on Saliva's Metabolome in Dental Medicine

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Abstract

New biomarkers for specific health conditions have been discovered as a result of the proliferation of metabolic research over time. One of the most recently and thoroughly developed bio fluids in the human body, saliva can be used as an informative substance for metabolomic profiling. The purpose of this review is to look at what is known about the human salivary metabolome, how it changes as a result of physiological, environmental and other factors, as well as the limitations and problems that have been found in the most recent research, with an emphasis on pre-analytical and analytical workflows. Additionally, we will investigate the possibility of using the saliva metabolomics profile as a biomarker for oral diseases like periodontitis and oral cancer.

Keywords: Metabolomic • Immunoglobulins • Rheumatologic • Oral sciences

Introduction

The biological fluid that is easily accessible from the oral cavity is saliva. It is produced by hundreds of minor glands in addition to three major pairs. The parotid, submandibular and sublingual glands are the three primary glands involved in the production of saliva, which are categorized as parotid saliva, submandibular saliva and sublingual saliva, respectively. The presence or absence of stimuli that trigger salivary secretion allows for additional classification. More specifically, the submandibular glands produce almost 70% of unstipulated saliva at rest, whereas the parotid glands produce the majority of stimulated saliva, which is induced by stimuli like smell, taste, or drugs. In the field of oral sciences, the transparent, clear, watery fluid that is made up of parotid, submandibular and sublingual saliva, in addition to the secretions of minor salivary glands, gingival crevicular fluid, eukaryotic cells (epithelial and leukocyte), food debris, microorganisms and their metabolites, is referred to as "Whole Mouth Saliva" (WMS).

Literature Review

Saliva is mostly water (99% of its composition) due to its aqueous composition. Other salivary products include salts, low molecular weight metabolites, digestive enzymes, growth factors, cytokines, immunoglobulins, antibacterial peptides, mucus and digestive enzymes. The average healthy person secretes between 0.75 and 1.5L of saliva per day, with more saliva being secreted while awake. Both within an individual and between individuals, the composition, flow rate and volume of saliva clearly differ. These variations are caused by stimuli that are sent by the autonomic nervous system's sympathetic and parasympathetic systems (neural control), as well as by physical, environmental, and/or pathological factors like circadian rhythm, age, gender, physical activity, oral hygiene, food consumption, medication and systemic diseases. Antibacterial and antiviral defence, lubrication and moisturization of the surfaces of the oral cavity, pharynx and oesophagus, oral digestion, tissue and tooth integrity protection and oral homeostasis are among its many functions [1].

The use of "omics" in medicine is the result of advancements in biotechnology and their applications in the health sciences. The appropriate conditions for circumstantial monitoring of smaller organ and/or cell compounds like proteins (proteomics) and low molecular weight metabolites (metabolomics) were established through the study of the structure, function, evolution and mapping of genes in genomics and transcriptomics, respectively. A metabolite is a tiny molecule that typically has a molecular weight of less than 1500 Da. The "metabolome" refers to the entire collection of small molecular metabolites. The most recent of the omics technologies, "metabolomics" investigates metabolites in bio fluids, cells and tissues [2].

The metabolomic profiling of a wide range of health conditions, including cancer, infectious diseases, neurological diseases (Alzheimer's disease, dementia), cardiovascular, rheumatologic, renal and respiratory disorders, is scientifically established and acceptable. Bio fluids found in the human body include serum, plasma, urine and cerebrospinal fluid. When it comes to salivary metabolites, on the other hand, there is very little evidence. The salivary metabolome is considered as a basic resource in clarifying pathways distinguishing different nearby and methodical problems and it could be utilized as a vital middle person in treatment plan and change as well as in treatment results. The point of this story survey is first and foremost, to reveal insight into the significance of the human salivary metabolome in wellbeing, optionally to evaluate the logical conventions and the impediments of salivary metabolomic studies and in conclusion to dissect the salivary metabolomic profile as a potential, adequate and strong biomarker of oral pathogenesis [3].

Discussion

The concentration of the healthy saliva metabolome is the primary focus of all salivary metabolomic research studies targeted or untargeted on healthy human samples. The most important factors that affect the healthy metabolome of human saliva are: the method of collection, in which stimulated saliva has a lower concentration of metabolites than unstimulated whole mouth saliva secretion samples; the type of gland from which the saliva is secreted, as submandibular gland saliva is more viscous than serous parotid gland saliva; gender; male saliva samples had significantly higher concentrations of acetate, formate, glycine, lactate, methanol, propionate, propylene glycol, pyruvate and taurine than female saliva samples; smoking status; the diurnal cycle (circadian cycle); specific salivary metabolites, primarily amino acids; and fasting conditions (diet); a longer period of time between the last diet and sample

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collection affected the salivary metabolomic profile and the At rest, the oral microbiome has a significant impact on the WMS's net metabolic composition and exposure to exogenous substances can alter that composition. According to the most recent research, some saliva metabolites have a strong correlation with the bacterial index of the WMS because certain WMS metabolites, such as short chain fatty acids (SCFAs), are not present in the sterile saliva of the parotid gland. Additionally, there are more inter-individual variations in the WMS metabolic patterns than there are in plasma metabolites. This may be due to the diversity of the oral microbiota that controls the WMS metabolites. Plasma metabolites, on the other hand, are easily controlled by host mechanisms. The dynamic interactions between various biofluids and the reflection of the oral microbiome on the salivary metabolome are additional areas of study [4].

According to a specialized perspective, a few insightful stages are formed and coordinated into the human spit metabolomic profiling process. The two most famous metabolite estimation innovations are atomic attractive reverberation spectroscopy (HNMR) and mass spectrometry (MS). Subcategories of MS strategies or extra combinatorial/conjunctive techniques are referenced beneath. Inductively coupled plasma mass spectrometry (ICP-MS), high performance liquid chromatography (HPLC), capillary electrophoresis time-of-flight mass spectrometry (CE-TOF-MS), gas-chromatography mass spectrometry (GC-MS) and liquid chromatography mass spectrometry. This brief review does not include a description of each analytical platform. Short-chain organic acids, amino acids, alcohols, amines, sugars and pharmaceutical adjuvants are all examples of compounds that can be identified and quantified using non-targeted NMR [5].

The fact that this method requires little to no sample pretreatment (deproteinization by centrifugation) and is more reproducible than MS analytical platforms are its primary benefits. MS, on the other hand, is a highly sensitive analytical technique that measures a substance's mass and number of ions using a variety of ionization techniques to identify and/or quantify it. Even at lower concentrations, the advantage of combining MS with other conjunctive methods is greater metabolite identification. The use of complicated separation and extraction steps to detect and analyze both polar and non-polar organic acids is highlighted as a problem that makes the mass spectrometry identification process more difficult. In contrast to NMR-based metabolomic analysis, MS-based metabolomics requires a well-designed pooled quality control sample (PQC) that is used for signal corrections throughout the sample batch. To make it clear that the complexity of the analytical instruments used in salivary metabolomic studies is another limitation, these characteristics are mentioned [6].

Conclusion

The majority of studies only employ a single analytical platform and attempt to analyse a single metabolome, rendering any potential comparison of salivary metabolic profiles among studies employing various analytical technologies meaningless. The use of the phrase "standard operating procedure" is of the utmost significance at this point. The use of pre-analytical, analytical and post-analytical methods is referred to by this term as the standardization and implementation of particular workflows. Sample pre-treatment (centrifugation for cell content removal and/or additional separation steps), sample analysis (by using more than one analytical platform), sample storage conditions (freezing temperatures), sample pretreatment (centrifugation for cell content removal and/or additional separation steps) and statistical methods used (principal component analysis partial least squares regression) would minimize the heterogeneous results in salivary metabolomic coverage caused by separation difficulties, sensitivity differences, instrument detection differences, compound stability, solubility, Scientific studies are categorized according to the quality and quantity of evidence that is available. This means that the quantity of evidence increases toward the base of the pyramid, but the quality of the evidence simultaneously decreases.

Acknowledgement

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Conflict of Interest

None.

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