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DETECTION OF MAGNESIUM IN SALIVA: CURRENT AND DEVELOPING METHODS

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Abstract: Identifying specific biomarkers for disease detection and using biomarkers to facilitate early diagnosis, which increases individuals' chances of survival, are among the most popular topics today. Magnesium, despite being among the most important of these biomarkers, is the least studied. These ions play a significant role in human physiological and pathological structures. Body fluids such as blood, urine, and sweat provide information about the human body. Magnesium, prominently present in saliva and abundant in the body, provides information about various pathological conditions, such as parotid malignant tumours, digitalis toxicity, chronic kidney disease, and dental enamel erosion. Information about diseases or their spread has recently become a significant source of interest due to the invasive nature of saliva and its promising potential for current clinical studies. Although numerous reviews on salivary biomarkers exist in the literature, this is the first systematic review specifically focused on Mg. This study examines the methods used to determine and quantify Mg in saliva, the studies conducted, and the results obtained. For this purpose, a systematic review of electronic databases was conducted, and studies from the last decade were reviewed, and current studies were compiled. The methods were evaluated under two main headings, each discussed separately. The health effects of the presented methods and their advantages and disadvantages are presented, providing a valuable contribution to the literature.

Keywords: Magnesium, Saliva, Health, Early diagnosis.

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1. INTRODUCTION

Early diagnosis, which increases a person's chance of survival, is associated with signals related to signs of the disease and their levels in biological fluids. The World Health Organisation (WHO) defines it as a measurement that reflects the interaction between any quantifiable element, metabolite, structure, process, or even a biological system that has the potential to affect or forecast the occurrence of diseases in the human body and potential hazard (Gug et al., 2019). The detection of these biomarkers varies according to the environment in which the detection is made (saliva, blood, etc.).

Fluids in the body, including blood, urine and sweat, provide various information about the human body. Saliva, among these body fluids, has a great place in biomedical studies with its various properties. Saliva is a water-based bodily fluid in the mouth produced by the salivary glands. Saliva, which contains 94-99% water in its composition, contains inorganic ions, secretory glycoproteins, serum elements and enzymes. Normal saliva is colourless, transparent, viscous, and tasteless (Diaz-Arnold & Marek, 2002; J. Pytko-Polonczyk1, 2017). Although the composition of saliva varies according to the body's structure, it provides information about many diseases. Saliva analysis has a wide range of applications, as it is non-invasive, can be easily collected, contains many biomarkers, can be easily stored, and maintains its stability for a long time (Woźniak et al., 2019). Hormone monitoring, detection of viruses such as HIV, hepatitis, COVID-19 (saliva-based PCR tests), diagnosis of cancer, dental health, diabetes follow-up, obesity and metabolic syndrome, DNA detection, epigenetics (Woźniak et al., 2019).

Typically, under natural conditions, Mg exists in the divalent form of Mg^{2+} and participates ionically in numerous biochemical reactions; for example, Mg is reported as a cofactor for over 300 enzymes (e.g., protein synthesis, energy metabolism, ion channel regulation). Comprehensive summaries and guides on the subject confirm this broad cofactor role (Jahnen-Dechent & Ketteler, 2012). Mg has a strong interaction with ATP: ATP molecules are often found chelated with Mg^{2+}, and the Mg ion plays a critical role in the structural stability of ATP and in many ATP-dependent enzyme reactions (e.g., phosphorus transfer reactions). This interaction highlights the indirect importance of Mg in cellular energy management(Posner et al., n.d.). Biophysiologically, antagonistic interactions between Mg and calcium (Ca) have been reported; Mg acts as a physiological Ca-antagonist by regulating membrane potential and Ca^{2+} fluxes. This antagonism has important consequences, such as in regulating smooth muscle tone, nerve, and cardiac function, and has been a long-discussed phenomenon in the literature(Jenkinson, n.d.). With the Mg ratio in saliva, important information can be obtained about diseases such as parotid malignant tumor, digitalis toxicity, chronic kidney disease (CKD), tooth enamel degradation in the mouth, cystic fibrosis, multiple sclerosis, and graft-versus-host disease (Aguiar et al., 2022; Aljerf & Mashlah, 2017) . In addition, stress lowers the level of Mg, which impacts the operation of the central nervous system (Proskurnina et al., 2023).

Figure 1, which provides a schematic representation of saliva composition and the biological role of Mg^{2+}, shows the main components of saliva. It also clearly illustrates the biological role of Mg^{2+} in saliva and the relationship between salivary components and Mg^{2+}.

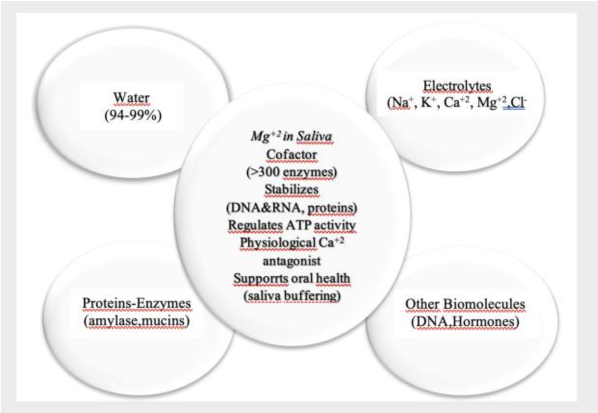

Figure 1. Schematic representation of saliva composition and the biological role of Mg^{2+}

The determination of magnesium in saliva has a long history and is gaining increasing attention in clinical and epidemiological studies (Table 1).

Table 1. Timeline of magnesium determination in saliva

Year	Method	Main Findings	Ref.
1935	Dialysis / adsorption (early chemical assays)	Early physicochemical studies reported calcium, phosphate, and magnesium in saliva; methodological limitations.	(Knox & Still, n.d.)
1955	Simple photometric / chemical methods	Practical methods for Ca and Mg determination in saliva were introduced; first standardized measurements.	(Ericsson, n.d.)
1965	Atomic Absorption Spectroscopy (AAS)	Mg levels have been shown to increase in paraffin-stimulated saliva.	(Gow, n.d.)
1968	AAS + ultrafiltration	Stimulated vs resting saliva fractions analyzed; Mg and Ca levels measured.	(Lear & Grin, 1968)
1979	Parotid saliva, flow rate, chemical assays	207 children: higher caries index linked to reduced Ca and P; Mg also decreased but less markedly.	(Shannon & Ralph Feller, 1979)
1994	Whole saliva / trace elements	The prevalence of dental caries in young adults is associated with salivary Zn, Cu, Ca, and Mg..	(Borella et al., 1994)
2018	Serum & saliva (Xylidyl blue method)	Mg levels significantly lower in OSCC patients compared to controls; potential biomarker role.	(Aziz et al., 2018)
2022	Salivary Mg in OSCC patients	Compared to controls, Mg differences were not consistently significant; mixed findings.	(Shekatkar et al., 2022)
2023	Calmagite method; serum vs saliva	In individuals with tobacco habits, Mg decreased with progression to potentially malignant disorders.	(Singhal et al., 2023)
2024	Serum & saliva (OSCC/OPMD vs controls)	Ca and Mg altered in OSCC/OPMD groups compared to healthy controls; Mg generally reduced.	(Samadi et al., 2024)
2024	Cross-sectional (IBD patients)	Inflammatory bowel disease patients showed significantly lower serum and salivary Ca & Mg vs controls.	(Mirzaii-Dizgah et al., 2024)

Liquid chromatography coupled with mass spectrometry (LC-MS) and ultraviolet-visible (UV-VIS) spectrophotometry, enzyme-linked immunosorbent assay (ELISA), electrophoretic immunoassay, radioimmunoassay (RIA), mass spectrometry-based proteomics, and DNA-based methods, microchips and microfluidic devices, and electrochemical biosensors are included in saliva biomarker detection (Gug et al., 2019). For Mg biomarkers, electrochemical, spectroscopic or biochemical analysis methods are generally used, but atomic absorption spectrometry (AAS) and ion-selective electrode (ISE) methods, fluorometric methods, ion chromatography (IC), voltammetric methods, chemosensors, inductively coupled plasma mass spectrometry (ICP-MS) and electrochemical techniques are used. These demonstrate the methodological diversity and the application potential of Mg determination in saliva (Table 2).

Table 2. Comparison of Mg determination methods

Method	Adv.	Disadv.	LOD/ LOQ	Ref.
AAS	High accuracy, reproducibilit; widely used standard method	Requires laboratory setup; time-consuming; skilled operator needed	µg/L	(Welz & Sperling, 1998)
ICP-OES/ MS	Multi-element analysis; very high sensitivity	Very expensive instruments; requires expertise; non-portable	ng/L	(Welz & Sperling, 1998)
Colorimetric Kits	Simple, rapid, low-cost; suitable for field applications	Relatively low sensitivity; potential interference effects	~40 µM	(Lewińska et al., 2024; Malahom et al., 2017)
ISE	Fast measurement; real-time detection	Limited accuracy; frequent calibration required	µM	(Bakker et al., n.d.)
Biosensors (enzyme/ aptamer-based)	High specificity; can be miniaturized; potential for field and clinical use	Stability and production cost issues; many still under development	nM–µM	(Guo et al., 2021; Stangherlin et al., 2025; Xu et al., 2023)
Microfluidic Paper-based Devices (µPADs)	Very low sample volume; low cost; rapid analysis	Fabrication techniques still under optimization; calibration may be required	µM	(Yetisen et al., 2013)

When we look at the reviews conducted to date, almost all of these studies aim to detect biomarkers in saliva. Saliva-based biomarker studies have generally focused on various analytes such as hormones, proteins, and nucleic acids (Gug et al., 2019; Woźniak et al., 2019). The need for the development of new techniques and methodologies for the determination of Mg in saliva is evident. However, despite magnesium (Mg) being one of the most critical cations for physiological functions, there is no review of studies specifically focused on the determination of Mg in saliva. Previous reviews have superficially addressed Mg as part of broader biomarker assessments or focused on its measurement in blood and serum samples (Diaz-Arnold & Marek, 2002; Ilea et al., 2019). This study, which stands out in many ways, fills this gap by systematically analyzing Mg determination in saliva, discussing both traditional and emerging techniques, and highlighting the clinical implications of measuring Mg in this biofluid. Its focus has established a rhythm in the literature. The methods are discussed, their advantages and disadvantages are discussed, and their effects on health development are attempted to be revealed.

2. MATERIAL - METHOD

This study compiled the literature on magnesium using a systematic review method. The screening process was carried out as follows:

A comprehensive literature search was conducted using PubMed/MEDLINE, Scopus, and Web of Science databases. Additionally, Google Scholar was used to identify open-access resources that were not indexed in primary databases. The search aimed to include the oldest studies on magnesium determination in saliva and the latest advances in biosensor technologies, particularly on studies conducted within the last 10 years. "Magnesium", "Mg^{2+}", "enzyme cofactor", "DNA stabilization", "ATP", "calcium antagonism", "Salivary magnesium," "salivary ions," "magnesium biosensors," "µPAD magnesium determination," "salivary electrolytes," and "analytical methods for salivary Mg" were used as search terms in the study. Boolean operators (AND/OR) were applied to maximise coverage. The types of studies are clinical, experimental, and in vitro studies. The study included (i) original research articles, (ii) studies reporting methods or technologies for the detection of magnesium in saliva, (iii) publications in English, and (iv) articles published between 2000 and 2025. (i) non-peer-reviewed sources, (ii) studies not explicitly related to magnesium in saliva, and (iii) conference abstracts without full text were excluded. After identifying relevant studies, articles were categorised for each method. The articles were reviewed in full text and evaluated under separate headings.

Which method will be used for the detection of Mg in saliva may vary according to the parameters of analysis sensitivity, cost, speed and laboratory facilities. While most of the studies were to identify various substances present in saliva (Ilea et al., 2019), it was observed that a limited part of them were focused on identifying Mg within saliva. The information obtained as a result of the searches made in electronic databases was evaluated and collected under 2 headings: detection methods, laboratory-based methods and methods under development.

2.1. Laboratory-Based Methods

Test kits, AAS, ICP-MS, and ion chromatography are among the laboratory-based methods.

First of all, when we look at the studies carried out with test kits, the study was based on the idea that exercise may lead to alterations in the biological indicators in saliva, and the selected saliva components were compared in swimmers before and after training. Of the 40 boys between 12 and 15, 30 were swimmers, and 10 were part of the control group. Saliva samples were taken from all participants in the morning and afternoon, and samples from swimmers before and after training. In the study, various parameters were measured, and a significant increase in Mg values was observed in swimmers following the morning exercise and after training in the afternoon. As a result of the study, it was concluded that magnesium levels were related to swimming training session (Grzesiak-Gasek & Kaczmarek, 2022).

Three groups were studied in which magnesium was estimated in serum and saliva. Groups studied: patients who use tobacco habit but not potentially malignant disorders, patients with tobacco habit as well as potentially cancerous conditions, and the control group. Mean saliva Mg levels were 1.442 mg/dl, 0.551 mg/dl and 0.463 mg/dl, respectively (Singhal et al. 2023). Enzyme-linked immunosorbent assay (ELISA) is the benchmark for biomarker identification and quantification in saliva (Pandit et al., 2024). However, the study in which the detection of

Mg was made with ELISA is quite limited. In a study involving 42 type II diabetic patients between the ages of 40 and 60 and 45 healthy controls without underlying systemic disease, the levels of saliva trace elements were evaluated using colourimetric and Ethylenediaminetetraacetic acid tests. It is stated that there exists a slight negative correlation between salivary magnesium and copper levels and CFU/ml, but this correlation is not statistically meaningful. Furthermore, it is stated that the mean saliva Mg concentration was 0.02121 ± 0.00445 in the study group, whereas the average concentration was 0.00062 ± 0.00006 in the control group (Mohammed et al. 2024). The disadvantage of the ELISA method is that it consists of many time-consuming steps, is expensive, and enables the examination of a single protein per plate (Gug et al., 2019).

Twenty subjects were included in the study, which evaluated stress biomarkers and electrolytes in the saliva of individuals receiving fixed orthodontic treatment. Saliva samples were collected at three different times, and Mg concentrations of electrolytes were evaluated using commercial kits. As a result of the study, when the saliva electrolyte composition was evaluated in the patient and control groups, it was stated that magnesium concentrations were similar in these groups (Silva Andrade et al., 2018).

AAS is a highly sensitive and accurate method for detecting Mg ions in saliva. The light absorption makes the detection of Mg atoms possible. To analyze the saliva sample, Mg ions are brought into atomic form by burning them in a flame or graphite furnace, and the concentration is calculated by measuring the amount of light absorption of Mg atoms at a specific wavelength. In the study, in which sodium (Na), potassium (K), Mg and Ca in human saliva were directly analyzed and their relationships with physiological states were examined, it was determined that the linear range for Mg was 0.0-0.5 mg/L and the LOD value was 0.5 mg/L. This study, which used the direct analysis method, stands out because chemicals were not used (dos Reis et al., 2020).

In the study using electrothermal atomization atomic absorption spectroscopy, it is stated that saliva Mg and parameters related to antioxidants can provide valuable insights in the examination of Generalised Anxiety Disorder (GAD). The study included 15 patients with GAD and 17 healthy individuals as volunteer control subgroups of the same age. Participants were subjected to a test at six difficulty levels, including false feedback. Participants were instructed to recall the colours of the balloons and respond when the colour shifted. The reaction time was interpreted by evaluating biochemical factors, including the antioxidant capacity of saliva and salivary magnesium levels, using the number of correct answers. It is stated that the Mg levels in saliva are elevated in patients with GAD than in the control group (Proskurnina et al., 2023).

In the study, which aimed to examine the connection between blood and salivary magnesium levels and pain characteristics and anxiety-depression scores in patients with migraine, 40 patients with migraine and 30 people without pain complaints as a control group were included in the study. The study concluded that saliva mg levels were reduced compared to the control group in both the attack and initiation periods. However, this low level was not related to pain characteristics. In addition, it has been stated that the initial and attack blood mg levels of patients with migraine are significantly lower than those with a long history of the disease (Altunkaynak et al., n.d.). Forty-two subjects used the study to compare gum health conditions and salivary magnesium levels in smokers and non-smokers. Saliva Mg levels were measured with AAS, and Mg levels were found to be 54.43±17.37 and 51.29±15.97 mg/dl in smokers and non-smokers, respectively (Wijaya et al., 2021).

ICP-MS involves ionizing the saliva sample, and Mg ions are separated by mass. With this method, even very low magnesium levels can be detected. In the study, in which individuals with type 2 diabetes were compared with a control group consisting of healthy subjects to analyze the levels of Mg, Ca, and zinc (Zn) in saliva, it was stated that the concentrations of Zn, Ca and Mg were significantly higher in the diabetes group than in the control group. In addition, it was noted that a relationship in ICP-MS involves magnesium levels in saliva ($p = 0.003$) in men. It is also among the results of this study that Mg, Ca and Zn levels in saliva may be useful markers to distinguish individuals with type 2 diabetes from those without diabetes (Marín Martínez et al., 2018).

In the study in which trace element levels in saliva were determined by ICP-AES in Oral Lichen Planus (OLP), a prevalent inflammatory condition of unknown origin, a study was conducted on 40 patients and 40 healthy individuals. As a result of the study, it was stated that Mg levels were notably reduced in patients with OLP compared to healthy controls, and there was no significant difference between erosive and non-erosive Lichen Planus types (Rezazadeh et al., 2019). In the study titled "The relationship between certain macro and trace elements in saliva and periodontal health", ICP-MS was used to determine the levels of the elements. A total of 190 systemically healthy, non-smoking participants (mean age 32.2 ± 6.02 years; 50 periodontally healthy controls (H), 50 patients with gingivitis (G), 50 patients with chronic periodontitis (CP) and 40 patients with disseminated aggressive periodontitis (GAP) were included in the study. As a result of the study, it was found that there was a significant difference in Mg concentrations between the groups, and that significant increases were observed in Mg, which is an essential mineral, ın both periodontitis groups, compared to the gingivitis group and periodontal healthy groups (Inonu et al., 2020).

Saliva samples from 66 healthy non-smokers (20 periodontally healthy, 24 untreated severe periodontitis, and 22 treated severe periodontitis patients were analysed using ICP-MS in the study, which aimed to compare the connection between mineral elements in saliva and periodontal health in patients with treated and untreated periodontitis with periodontally healthy controls. In healthy controls, Mg levels in saliva were found to be 6.31 ± 0.59 mg/L, 7.67 ± 1.013 mg/L, and 6.125 ± 0.78 mg/L in untreated periodontitis and treated periodontitis (Romano et al., 2020).

In the ion chromatography method, in which Mg is measured by separating it from other ions, the concentration is determined by separating the Mg ions in the saliva sample from other ions using chromatographic columns. It has the advantages of high solubility and specificity, being suitable for use in complex biological fluids. In the study, where the piezoelectric quartz crystal (PQC) detector was created and the Calcium (Ca^{2+}) and magnesium (Mg^{2+}) levels in human saliva and urine were determined by ion chromatography, some samples were also determined by the AAS method. The t value obtained in the method used was 3.42 for Mg in saliva (Yu et al., 2001).

2.2. Methods Under Development

ISE, chemosensors, microfluidic-based structures and biosensors are included in this heading.

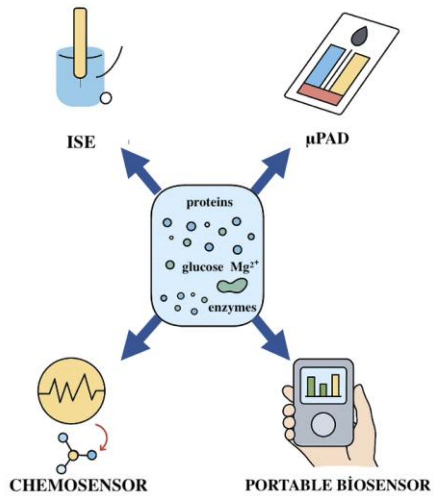

Figure 3. Illustration of methods under development

It is based on the principle that ion-selective electrodes detect a specific ion through a selective membrane. Electrodes that selectively detect magnesium ions in saliva provide fast and practical analysis. Different electrodes can be used, such as graphite electrodes or screen-printed electrodes. It is easy to apply, gives quick results, and can be done with portable devices. The study shows the possibility of using ISEs for ionic component changes in saliva in saliva samples by determining various ion concentrations, such as Sodium (Na+), potassium (K+), calcium (Ca^{2+}), magnesium (Mg^{2+}), and chloride (Cl-) using glassy carbon-based ISEs and a sensor platform with glassy carbon electrodes. It is also noted that there is a connection between the type and intensity of body stimulation and the ion concentration (Urbanowicz et al., 2017).

In another study in which salivary magnesis levels were estimated ın individuals with oral squamous cell carcinoma, it was stated that impaired Mg homeostasis would lead to pathological conditions. Based on the change in the level of Mg in saliva in patients with cancer, a study was conducted on 36 people, 18 of whom were sick. While the Mg level was 0.4333 mg/dl in the control group, this level was 0.5778 mg/dl in patients (Shekatkar et al., 2022).

Chemosensors create signals by interacting with magnesium ions. In addition to being usable for detecting Mg in biosensors and similar devices, it is sensitive and portable. µPADs stand out with their ability to enable on-site detections, trained operators and the fact that they do not require special laboratory equipment. In the study, in which a microfluidic paper-based analytical device (µPAD) was created for the determination of Mg in saliva samples, magnesium standard solutions within the range of 0.082-0.247 mM were prepared with synthetic saliva and Bovine serum albumin (BSA), and the colour intensity was measured through image processing. The limits of detection and quantification are 62 µM and 81 µM, respectively (Aguiar et al., 2022).

Biosensors, simply put, are analytical devices consisting of a bioreceptor, a transducer, and a signal processor for identifying molecules (Rezazadeh et al., 2019). They consist of two main components: a bioreceptor and a transducer. The bioreceptor is responsible for analyte recognition and the sensor's broad specificity and sensitivity. They can bind to a specific substrate and are categorised into three groups: enzyme-based, whole-cell-based, and bioaffinity-based (Mehrvar et al., 2000). Biosensors are widely used in various fields such as health monitoring, environmental analysis, food safety, etc. Various transducers, such as electrochemical transducers, optical transducers, and piezoelectric transducers, can be used in its structure, and the sensors take different names according to the transducer structure used. Electrochemical sensors, a type of biosensor, are widely used in clinical applications for detecting biomarkers in saliva, their effectiveness, and diagnostic/therapeutic applications due to their low cost and fast analysis features (Zheng et al., 2021). The electrical changes caused by Mg ions on the electrode are detected. Fast and low-cost, it can be applied in portable devices.

When the literature is evaluated, it is observed that several studies exist involving biosensors and Mg duo. For example, in biosensor studies where saliva-based or saliva-based biomarkers can be detected, it is seen that the detection of lactate, glucose, phosphate, salivary hormones, etc., is emphasized (Malon et al., 2014). In many studies, Mg stands out as a component used in producing biosensors rather than being an analyte to be detected by biosensor structures (Kao et al., 2017; Vladimirov et al., 2014; Yang et al., 2023). The most important conclusion to be drawn from this is the necessity of contributing to the literature in this field.

A microfluidic paper-based analytical device (μPAD) has been developed to determine magnesium in saliva samples. This device is based on the principle of magnesium forming a colored complex with eriochrome cyanine, and analysis is performed by measuring colour intensity using digital scanning. The device has a lower detection limit of 62 μM, providing a user-friendly solution that does not require laboratory equipment (Aguiar et al., 2022). The integrated microfluidic immunosensor device combines vibration-accelerated incubation and magnetic separation technologies. This device is designed for rapid and sensitive biomolecule detection and can be used in biological samples such as saliva(Liang et al., 2025). Artificial intelligence-supported biosensors have been developed to assess the homogeneity and stability of sodium, calcium, magnesium, and manganese ions in saliva. These sensors play an important role in the detection and analysis of biomarkers(Constantin et al., 2025).

These studies demonstrate the diversity and advancements in biosensors and microfluidic systems developed for detecting magnesium in saliva samples. These technologies are expected to be further developed and widely used in clinical applications in the future.

Table 3. Comparison of under development methots

Method	Adv.	Disadv.	LOD	Detection Time	Portab.	Ref
μPAD	No laboratory required, low cost, user friendly, fast and practical	Possible error in color measurement, limited accuracy, analysis time may be long under some conditions	62 μM	10–90 min	High	(Aguiar et al., 2022)
Integrated Microfluidic Immunosensor	Fast, accurate, low-cost, portable	Limited mechanical durability, sensor life may be shortened, manufacturing process may be complicated	0.57 μM	5 sec	Medium	(Wang et al., 2025)
Smartphone-Based Biosensor	Portable, user-friendly, digital data recording	Variation in color measurement due to camera, limited sensitivity	50 μM	1 min	High	(Awad et al., 2025)
AI-Supported Biosensor	Multi-ion detection, strong data analysis capability	Requires AI model training, relatively expensive	–	–	Medium	(Constantin et al., 2025)

3. CONCLUDING REMARKS AND FUTURE PERSPECTIVES

Determining the concentrations of various minerals, elements, enzymes and hormones in human body fluids in a short time with high sensitivity plays a crucial role in detecting and evaluating the disease. This situation has brought with it a continuous increase in the need for advanced technology and sensitive analysis methods. In addition to the increase in the variety and number of diseases, the proportional rise in cancer and psychological disorders underlines that the need for this situation is gaining importance day by day. Determination and monitoring of Mg in body fluids is significant because there is currently no quick and straightforward test to assess total body magnesium.

Saliva has important advantages with its features of being non-invasive, painless, easy to sample, low cost, and not requiring long processing. Considering its content, saliva is promising in the early detection and management of many diseases.

Based on all these cases, this study highlights the methods and developments in magnesium detection in saliva. The magnesium detection methods reviewed in this review have the potential to measure magnesium with high sensitivity, particularly in saliva and other biological fluids. A brief evaluation of the studies in the literature is presented in Table 4. While existing methods provide reliable results in the laboratory setting, some challenges remain regarding integration into clinical practice. For example, the complex instrumentation requirements and long analysis times of traditional techniques limit their use in routine patient care. Laboratory-based methods have many processing steps, require expensive and complex devices, and do not provide results that enable rapid, sensitive, and early diagnosis. Furthermore, the requirement for short-term storage at specific temperatures in saliva to prevent degradation remains an unresolved issue. In the future, portable biosensors may be critical for magnesium monitoring

in clinical practice. Such devices can support individual health management by providing fast and accurate data at the patient's bedside and in remote healthcare settings. Portable devices will have a significant impact, particularly in chronic disease monitoring, nutritional assessment, and athletic fitness monitoring. Research gaps focus on clinical validation, data standardisation, and accessible portable device design.
It is known that more sensitive determinations are needed, such as the determination of magnesium, a biomarker in saliva. In this regard, biosensor structures often come to the fore. This necessitates designing and implementing green biosensors that will not harm the environment and allow for rapid, sensitive, and cost-effective detection. This will facilitate disease diagnosis and monitoring while contributing to the development of healthcare services. Easier sample collection in the elderly and children will enable large-scale screening.

Unlike previous studies, this review focuses solely on determining Mg in saliva, whereas in previous studies, it was treated as a secondary analyte. By systematically compiling and comparing existing methods, our study offers a unique perspective not previously addressed, thus contributing to the literature.

Furthermore, developing environmentally friendly biosensors is important for cost and sustainability. Replacing traditional sensor materials with biological or biodegradable components will provide ecological advantages for laboratory and field use. This approach will increase the applicability of biosensor technology not only in the healthcare sector, but also in environmental monitoring and food safety. Standardisation and validation efforts should be increased to ensure reliable operation of sensors in hospital and home environments for clinical integration. Translating data obtained from portable devices into individual risk assessments using artificial intelligence and machine learning is crucial for data analytics and digitisation. Multi-analyte sensor systems can be designed by developing systems that enable the simultaneous detection of not only Mg^{2+} but also electrolytes such as Ca^{2+} and K^{+}. Future research gaps exist in increasing healthcare accessibility in low-income areas through inexpensive, portable, and user-friendly sensor designs. In light of these perspectives, the applicability of magnesium measurement technologies not only in basic science and laboratory research but also in clinical and daily life will significantly increase. This will create new opportunities for individual health management and public health policies.

The differences in speed, sensitivity, cost and applicability of the methods used to determine magnesium were shown in tabular form and then interpreted graphically.

Table 4. Studies in the literature

Method Used	LOD/LOQ	Time	Advantages	Disadvantages	Ref.
Sequential Injection	1–5 mg/L	3 min	Fast measurement; relatively simple automation	Limited sensitivity; requires specialized equipment	(Machado et al., 2018)
EDTA titration and ISE	1.2–4.5 mg/L	-	Inexpensive; classical and well-known methods	Low sensitivity; operator-dependent; not suitable for very low Mg levels	(Aljerf & Mashlah, 2017)
µPAD	82–247 µM (62 µM)	10–90 min	Portable; low-cost; suitable for point-of-care	Longer analysis time; lower precision compared to lab-based methods	(Aguiar et al., 2022)
Coral Magnesium Kit	-	5 min (collection) + 10 min (centrifuge)	Easy-to-use; can be applied in clinical settings	Moderate sensitivity; influenced by patient habits (tobacco/alcohol)	(Singhal et al., 2023)
Colorimetry	0.02121 ± 0.00445 mg/L (working group)	Prep: 2 h, Meas: 40 min	High sensitivity; relatively low cost	Time-consuming; prone to interference; needs careful preparation	(Mohammed et al., 2024)
Commercial Kit	-	5 min	Very quick; user-friendly	May lack accuracy; variability across kits	(Silva Andrade et al., 2018)
AAS	2.57 ± 0.06 mg/L; 0.5443–0.5129 mg/L	5–80 min	High accuracy and reproducibility; widely validated	Requires laboratory, expensive instruments, trained operator	(dos Reis et al., 2020; Wijaya et al., 2021)
ICP-MS	~0.01–0.1 mg/L (very low)	Prep: 10 min, Meas: 12 min	Ultra-sensitive; multi-element detection	Very high cost; requires laboratory; complex operation	(Romano et al., 2020)
Xylidyl Blue Method	-	16 min	Relatively fast; colorimetric simplicity	Interference from other ions; limited precision	(Shekatkar et al., 2022)
Xylidyl Blue Method (variant)	-	-	Allows differentiation of health vs malignant disorders	Limited comparability; moderate sensitivity	(Aziz et al., 2018)
Spectrophotometers	-	-	Widely available; simple analysis	Low specificity; limited sensitivity	(Al-Abdaly et al., 2021)

A radar chart was created to compare methods simultaneously according to multiple criteria, such as LOD/LOQ, time, cost, and portability, and to visualise their strengths and weaknesses holistically. At this stage, data for the methods' four different parameters (LOD, time, cost, portability) were determined. Because each parameter has different units, all values were normalised to the 0-1 range. The radar chart in Figure 4 was then created.

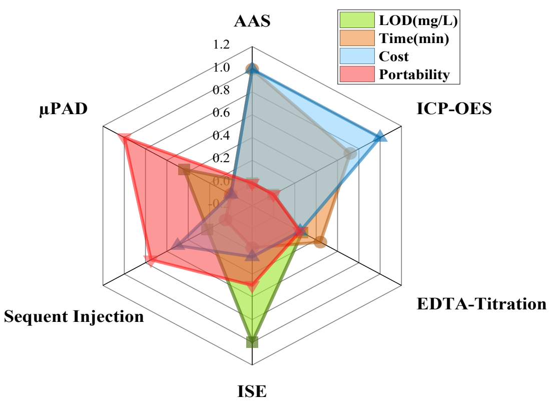

Figure 4. Multicriteria comparison of magnesium detection methods

Looking at the graph, the method with the lowest LOD value is more pointed than the others. This method offers high-sensitivity (low LOD) measurement. Methods with narrow red zones are more portable (more suitable for field applications), while those with wider red zones are laboratory-dependent. Methods closer to the centre are both faster and more cost-effective.

When the methods are evaluated, μPADs are preferred for clinical use, where speed and practicality are important. AAS or ICP-MS are preferred for research and laboratory settings where sensitivity is high. μPADs or portable ISE devices are preferred for screening and field studies, where portability and low cost are important. ICP-MS is preferred for biomarker studies. As can be seen from the graph, rather than determining a single "best" method, the criteria by which each method stands out are visually highlighted. Some methods are very sensitive (good LOD) and fast, but compromise on portability and low cost, while others are less expensive and portable, but have lower sensitivity.

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The authors have no conflicts of interest to declare.

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