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Review Article

Current Status of Component Analysis of Urinary Calculi

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Abstract

Urinary calculi are prevalent urological disorders, and their prevalence is rising globally. Thus, early detection, diagnosis, treatment, and prevention of stones are critical. Optical polarization microscopy, scanning electron microscopy, element distribution analysis, wet chemistry, thermogravimetry, X-ray powder diffraction, infrared spectroscopy, and artificial intelligence are currently used to analyze the composition of urinary calculi. Stone composition analysis was utilized to estimate stone prognosis and recurrence, with the goal of improving stone prediction and prevention. This research is an important component of customized therapy and stone recurrence prevention, offering a new approach to clinical diagnosis and treatment of urinary calculi. This review focuses on the current research advances in the composition analysis of urinary calculi and its impact on the treatment and prevention choices for urinary calculi, as well as its value in clinical application.

Keywords: Stone Composition Analysis; Stone Prevention; Urinary Calculi

Introduction

Urolithiasis is a genitourinary illness characterized by the presence of urinary calculi throughout the urinary tract. The most common clinical symptoms were exercise-related pain and hematuria. Urinary calculi are a highly widespread condition that has recently become more common over the world. Its makeup is complex and changes depending on geography and individual characteristics. According to the literature, 1-20% is the estimated global incidence of urolithiasis[1-3]. It is more prevalent in those whose diets include a lot of meat, although it is uncommon in vegetarian and vegan communities [4]. In terms of geographical distribution, the disease is most common in Western nations like the United States (13–15%) and Canada (12%); in European nations, the range is significantly lower (5–9%), while in East Asian nations like Japan (1%–5%), it is rare [5]. The incidence of urolithiasis in China ranges from 1% to 5%, with the southern region having a much greater incidence than the northern region, with a peak incidence of approximately 10% [6]. The Middle East has the largest risk of morbidity, which can range from 20 to 25% because of the region's environment, which promotes prolonged sun exposure, higher production of vitamin D3, and increased daily skin fluid loss [5]. Globally, urolithiasis incidence has increased recently, with a maximal recurrence rate of more than 50% in 5 to 10 years [7]. Currently, it is thought that urolithiasis affects individuals between the ages of 30 and 60 and is more common in manual laborers. It also affects men more frequently than women, however the gap between the sexes has been gradually closing in recent years [8, 9]. In addition, a number of other factors, including genetics, nutrition, geography, and climate, might influence the development of urinary calculi. These factors can also affect the clinical features of the various calculi components. Since calcium is the main component of over 75% of stones, it is the most prevalent component in urolithiasis [10]. The majority of urolithiasis is made up of roughly 70–80% calcium phosphate and oxalate, 10% uric acid, 10% struvite (magnesium ammonium phosphate), and fewer than 1% cystine or drug stones [11]. The etiology of urolithiasis is multifactorial, and a crucial consideration in comprehending the formation process of stones and devising prophylactic treatment approaches is their composition. Significant strides have been achieved in the last several decades in the analysis and investigation of the composition of urinary calculi, which has improved our knowledge of how calculi arise and how to treat them. Comprehending the makeup of urolithiasis is also crucial for directing therapy choices and prophylactic actions. Currently, the only way to accurately detect the composition of a stone is in vitro. Following the collection of stone samples, the stone composition of the removed stone fragments is often determined and analyzed using X-ray diffraction, or Fourier Transform Infrared (FTIR) spectroscopy [12, 13]. Urologists have therefore generally focused on preoperative prediction of stone composition in the body using quick and noninvasive procedures, as this is crucial for the diagnosis, management, and avoidance of urolithiasis recurrence. This paper learns about the pertinent literature and summarizes the stone composition and analysis methodologies, which are presented as follows, in order to investigate the current research status of stone composition analysis.

Current Research Status of Main Components of Urinary Calculi

Currently, urolithiasis is classified into three categories based on etiology: non-infectious stones, infectious stones, and stones linked to genetic abnormalities, under the European Association of Urology's urolithiasis guidelines, 2023 edition [14]. Non-infectious stones include: calcium oxalate stones, calcium phosphate stones, uric acid stones. Infected stones include: magnesium ammonium phosphate stones, highly carbonated apatite, ammonium urate stones. Genetic defects associated with stones include cystine stones, xanthine stones, and 2,8-dihydroxyadenine stones.

- **Calcium Oxalate Calculus:** This product, which primarily consists of calcium oxalate, is typically linked to irregular oxalate metabolism. The principal constituents consist of calcium oxalate dihydrate and monohydrate, which are primarily observed as mixed stones [7]. Many variables, primarily related to excessive oxalate concentration, aberrant calcium salt concentration, supersaturation and pH, and insufficient stone formation inhibitory factors, interact to generate calcium oxalate stones. With the help of alkaline citrate, one can effectively avoid the recurrence of calcium oxalate stones by inhibiting crystal aggregation and development, increasing the concentration of citrate in urine, and reducing the supersaturation of calcium oxalate, calcium phosphate, and urate in urine.

- **Calcium Phosphate Calculi:** The primary constituents of calcium phosphate calculi are calcium carbonate and hydroxyapatite, and they have aggressive and highly recurrent properties [15]. Numerous factors have been linked to the production of calcium phosphate stones, as evidenced by studies, with hypercalciuria, hypocitraturia, and high urine pH serving as key risk factors [16]. The main causes of calcium phosphate stones include Renal Tubular Acidosis (RTA), Hyperparathyroidism (HPT), and Urinary Tract Infections (UTI). Treatment of the primary disease helps prevent the recurrence of stones. Thiazides are advised for patients with calcium phosphate stones who have elevated urine calcium concentrations because they lower urinary calcium concentrations and prevent intestinal effects on calcium absorption.

- **Uric Acid Calculus:** Uric acid makes up the majority of uric acid calculus.Uric acid stones are thought to be primarily caused by low urine pH (below than 5.5), in contrast to calcium stone types [17]. One metabolite that is created when the body breaks down purine in meals is uric acid. The kidneys filter out the majority of uric acid, which is then expelled in the urine. Uric acid, however, crystallizes and eventually turns into uric acid stones when the quantity of uric acid in urine is too high or when the solubility of uric acid in urine diminishes. Uric acid stone risk factors include obesity, hyperlipidemia, hyperinsulinemia, and hyperuricemia. Oral medicines are effective in treating uric acid stones; they are not effective in treating sodium urate or ammonium urate stones. The fundamental idea behind oral medication-assisted stone dissolving is the alkalinization of urine using sodium bicarbonate or alkaline citrate. During treatment, the pH of the urine should be kept between 7.0 and 7.2. While uric acid dissolves more quickly in a higher pH, this may also encourage the development of calcium phosphate stones. Individuals who self-monitor the pH of their urine must modify the dosage of alkalinizing medications [18, 19].

- **Infected Stones:** Around 7–8% of all stones are infected globally, and they are typically brought on by an increase in ammonia production brought on by urease-producing bacteria like Klebsiella or Proteus [7]. A unique class of urinary calculi are infected stones, which mostly consist of ammonium urate, highly carbonated apatite, and magnesium ammonium phosphate stones. According to reports, there is a significant chance of infectious complications after surgery for infectious stones. These complications might result in potentially fatal illnesses like sepsis and septic shock [20-22]. In order to prevent urinary tract infections before surgery, sensitive antibiotics must be regularly used. If the anti-infective action is ineffective or associated with hydronephrosis infection, ureteral stent drainage or percutaneous nephrostomy drainage can be established as needed [14, 23, 24]. Urease inhibitors, which are used to treat infections, can also be used to prevent the formation of infected stones by acidifying urine with ammonium chloride [21]. Preventing urinary tract infections and routinely assessing the composition of urine are crucial in preventing the development of infectious stones.

- **Cystine Stones:** Autosomal recessive abnormalities in the renal transporter of the amino acid cystine cause cystine stones [25]. Cystine is a very important amino acid and is usually present in a stable form in urine. Normally, the kidneys should totally reabsorb it, and it shouldn't show up in the urine. However, because the body lacks transporters for normal cystine, patients with the hereditary condition cystinuria have higher quantities of cystine in their urine, which makes it impossible for the kidney to reabsorb cystine correctly. [26]. Stones are formed when crystals start to form as a result of cystine being oversaturated. A low-protein diet can lower cystine excretion, and excessive consumption of methionine-rich foods (soybeans, wheat, fish, meat, beans, and mushrooms, etc.) should be avoided. In order to cure cystine stones, urine need to be alkalinized to a pH greater than 7.8, and captopril inhibits the development of cystine stones.Urinary calculus composition is still being studied, and scientists are working hard to understand how metabolic disorders, genetic factors, and stone formation mechanisms are related. The pathophysiology of urolithiasis is better understood due to these investigations, which also advance the creation of therapeutic and preventive approaches and improve clinical management.

Methods for analysis of urinary stone composition

- **Polarizing microscopy:** The basis of this method is the way polarized light interacts with stone crystals. A drop of the proper refractive index fluid can be used to evaluate the stone under a polarized light microscope after it has broken and material has been removed from its tip [27]. Stone minerals can be distinguished by its color, light refraction, and double refraction, among other characteristics. This method offers helpful data for determining the kind and composition of stone in an initial sense [28]. It has the advantage of being able to analyze stones that are too small to be used for other analytical procedures and provides a clearer description of the stone than the sum of cationic and anionic components supplied by chemical analysis [27].

- **Scanning electron microscopy:** Scanning electron microscopy is an accurate method for studying the morphology of urinary calculi. And this procedure is non-destructive, revealing features of stones ranging in size from 1 to 5 nm without altering the complex's particular form [29]. Furthermore, when compared to conventional light microscopy, it can provide very high-resolution sample surface pictures, making it more suitable for observing stone sample structure.

- **Elemental Distribution Analysis (EDAX):** In addition to being extremely helpful for recognizing unknown crystals that cannot be detected by standard light microscopy alone, it is utilized to determine the composition percent of elements in all stone samples. The results of scanning electron microscopy may be verified, the shape and crystal structure of different sediments can be examined, and the percentage of each element present in the sample can be determined using elemental distribution analysis [30]. The generalization of these technologies to include equipment availability and cost of use is limited, though, by the fact that this technology is not frequently employed in clinical settings [21].

- **Wet Chemical Analysis:** Wet chemical analysis is a common stone analysis approach in ordinary laboratories, although it is limited to detecting the presence of individual ions and free radicals [29]. As a result, it may not be able to differentiate between particular chemicals in complicated stone kinds and mixes. According to data from the External Quality Assurance Scheme (EQAS), wet chemistry techniques, both qualitative and semi-quantitative, including kits that are sold commercially, have demonstrated comparatively low performance in practice. better results when applying wet chemistry in a quantitative manner [29]. This method's drawback is that it cannot handle small sample sizes of stones because it needs at least 10–15 mg of sample to handle rare and unknown components.

- **Thermogravimetric Analysis (TG Or TGA):** Since the 1970s, thermogravimetric analysis has been extensively employed in the examination of renal calculi [31]. Because thermogravimetric analysis can yield fast, quantifiable results, Rose GA et al. [32] recommended using it for stone analysis. Thermogravimetric analysis is a practical, quick, and easy method that relies on continuously monitoring the material's temperature and weight loss as it is gradually heated to 1000°C in an oxygenated environment. The nature of the substance will be revealed by a weight change pattern, and the size of this change shows a proportion because each substance has a unique type of transformation, transformation start and finish temperatures, quantity of weight change, and enthalpy [29]. This method's drawbacks include the comparatively high material requirements for compositional analysis's ideal resolution and the incapacity to recycle samples for further usage. Nevertheless, when heated, calcium phosphate, silica, and calcium pyrophosphate exhibit negligible weight changes, making thermogravimetry insufficient for their definitive identification. Instead, further quantitative wet chemistry techniques should be employed to corroborate their identification [29].

- **X-Ray Powder Diffraction (Xrd):** a method that uses X-rays that diffract when they come into contact with atoms in a crystal that are close together, and then analyzes the patterns that are produced to identify the characteristics of the crystal [33]. This technique can detect crystalline material or mixes of crystalline material, however non-mineral components (proteins and matrices) and amorphous calcium phosphate may occasionally be present and unidentifiable [29]. X-ray powder diffraction is more reliable and requires less effort than infrared spectroscopy; yet, it is more expensive and cannot study amorphous compounds[34].

- **Infrared Spectroscopy:** The application of infrared spectroscopy dates back to1955[35]. Infrared spectroscopy is the process of applying infrared light to a sample at successive frequency variations, causing the molecules to absorb energy at certain frequencies and create curves with certain wavelengths [36]. But over the past ten years, it has developed into a widely accepted and trustworthy technique for quantitative analysis of stones in vitro. Infrared radiation is used in a precise, quick, and adaptable manner to cause atomic vibrations and, ultimately, energy absorption. As a result, absorption bands eventually show up in the infrared spectra of stone samples[29]. Stone specimens were combined with potassium bromide and compacted into discs for examination using direct infrared transmission. As a result, stone specimens could not be obtained for for further supportive study, including wet chemical analysis[29]. Specimens can be retrieved, nevertheless, using nondestructive techniques such photoacoustic detection[37]. The Attenuated Total Reflectance (ATR) approach is a more recent infrared spectroscopy technique that works well with soft samples[28]. Furthermore, this technique requires relatively little preparation of the specimen because it does not require mixing the specimen with infrared inactive compounds like potassium bromide before analysis[10]. This method, as opposed to X-ray diffraction, can identify amorphous materials, such as amorphous fatty material, and assist in identifying the organic stone constituents, including purines and drug metabolites.

- **Artificial Intelligence Prediction of Stone Composition Model:** Artificial intelligence is increasingly being used in medicine, particularly to anticipate the composition of stones. Early investigations of artificial intelligence used to deep learning for lesion identification or classification shown superior performance to traditional techniques, even outperforming radiologists in several tasks [38]. These models are typically built using medical imaging data including X-rays, CT scans, and ultrasound pictures. Artificial intelligence algorithms can analyze these photos to determine the kind and content of stones. Kim US et al. [39] demonstrated the feasibility of deep learning for diagnosing urinary stone composition using pictures. Kazemi et al. [40] used Bayesian model decision-making, ANN, and rule-based classifiers to detect kidney stone kinds and the most influential characteristics, achieving an overall model accuracy of roughly 97.1%. X Cui et al. [41] employed image-omics to differentiate infectious stones from non-infectious stones based on contrast-enhanced CT images, employing the bagged trees machine learning technique, with a model accuracy of 90.7%, sensitivity of 85.81%, and specificity of 93.96%. These artificial intelligence prediction models can be utilized as an alternate tool for routine stone analysis, assisting urologists with decision-making and improving diagnosis and treatment efficiency.

Application of Composition Analysis in Prediction and Identification of Urinary Calculi

Component analysis of urolithiasis is critical for prognosis, diagnosis, and treatment planning. Understanding the composition of stones can assist clinicians in determining the most appropriate treatment and preventing stone recurrence. Understanding the composition of stones can help to tailor treatment plans. Compositional analysis can determine the specific composition of stones, including oxalate, uric acid, and cystine. Depending on the content of the stone, the physician may determine the best treatment. For example, infectious stones frequently necessitate antibiotic intervention [7], but uric acid stones can be treated with allopurinol or febuxostat [42]. Knowing the stone's composition also helps to prevent its recurrence. To lessen the risk of stone reformation, physicians may counsel patients to make appropriate lifestyle and dietary adjustments based on the kind of stone and its composition. Uric acid stones, for example, prevent uric acid buildup by increasing urinary flow. Increasing fluid intake can boost urine output, lowering the supersaturation condition of several stone components in urine and thereby preventing stone recurrence [43]. By studying a significant number of urinary stone composition data, researchers can gain a better understanding of stone epidemiology and etiology, allowing for better prediction and prevention. This study is an important part of individualized treatment and prevention of stone recurrence.

Prospects for Future Studies on Composition Analysis of Urinary Calculi

Future research views on the composition analysis of urinary calculi are promising, and with the advancement of science and

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technology, we can anticipate to witness greater progress. With the advancement of technologies like as genomics, proteomics, and metabolomics, we may anticipate that urolithiasis component analysis will be integrated with individual genetic information to customize drug therapy for patients with polygenic genotypes [44]. By evaluating the patient's genetic information, clinicians can forecast the patient's risk of stone formation and devise more specific prevention and treatment techniques. At the same time, researchers expect to discover previously unknown components in stones using advanced analytical techniques. The discovery of novel components will open up new avenues for the prevention and treatment of urinary calculi, allowing us to better understand the mechanism of stone formation and develop new drugs or therapies. With the advancement of science and technology, the use of big data and artificial intelligence will undoubtedly cause a revolution in research. By gathering large-scale clinical data, along with artificial intelligence algorithms, researchers may evaluate more complicated patterns and trends, providing more accurate results for component analysis of urinary calculi [39, 45, 40, 41]. This is also expected to speed the research process and increase its efficiency. Researchers can discover the law and trend of stone production by analyzing huge amounts of data, providing a scientific foundation for the development of more effective preventative techniques. This could involve tailored treatment options for high-risk groups, as well as assistance with diet suggestions and lifestyle adjustments to help patients lower their risk of developing stones.

Conclusion

The composition of urinary calculi is a useful tool for determining the cause and guiding treatment. Current research has demonstrated that the composition corresponding to different forms of urolithiasis varies; thus, accurate and reliable analysis methods are required for tailored therapy and prevention. Future research should focus on the use of emerging technology and the creation of personalized treatment strategies to improve urinary calculi prevention and therapy.

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