Infrared spectroscopy is the gold standard for kidney stone analysis

Urinary stones can be caused by a variety of underlying disorders or diseases. Acquiring knowledge of the urinary stone constituents is important in order to offer stone-specific treatment, to reveal the aetiology of stone formation, and to ensure optimal individualised prophylactic treatment to prevent recurrence. Kidney stone analysis is recommended in the basic evaluation of stone disease. Infrared spectroscopy is regarded as the gold standard for stone analysis.

Urinary tract stone disease (urolithiasis) is a common disorder. In Norway, 10–15 % will suffer one or more stone attacks during their lives. Men have twice as high a risk as women. The prevalence of stone disease is increasing, presumably due to increased incidence of obesity, metabolic syndrome and type 2 diabetes (1, 2), as well as increased intake of animal protein and salt, and reduced intake of calcium (3, 4). There is a considerable risk of stone recurrence, since approximately 50 % will suffer a new attack within 5 years of their first stone episode and 70 % within 20 years. Among stone formers, about 10 % have highly recurrent disease. Loss of kidney function and infection, such as urosepsis, are potentially severe consequences of urinary stone disease.

Extracorporeal shock wave lithotripsy (ESWL) and the minimally invasive stone removal procedures ureterorenoscopy (URS) and percutaneous nephrolithotomy (PCNL), which have been used in the management of stone disease for the last 30–35 years (5), may have contributed to a reduced focus on prevention of stone recurrence. In Norway, analysis of kidney stones is presumably underused. This is unfortunate, as prevention of stone recurrence is important to reduce the morbidity of the individual patient, and efficient prevention also leads to reduced costs, as fewer stone removal procedures are required.

«Infrared spectroscopy can be used to determine the relative percentage content of the various components with high accuracy»

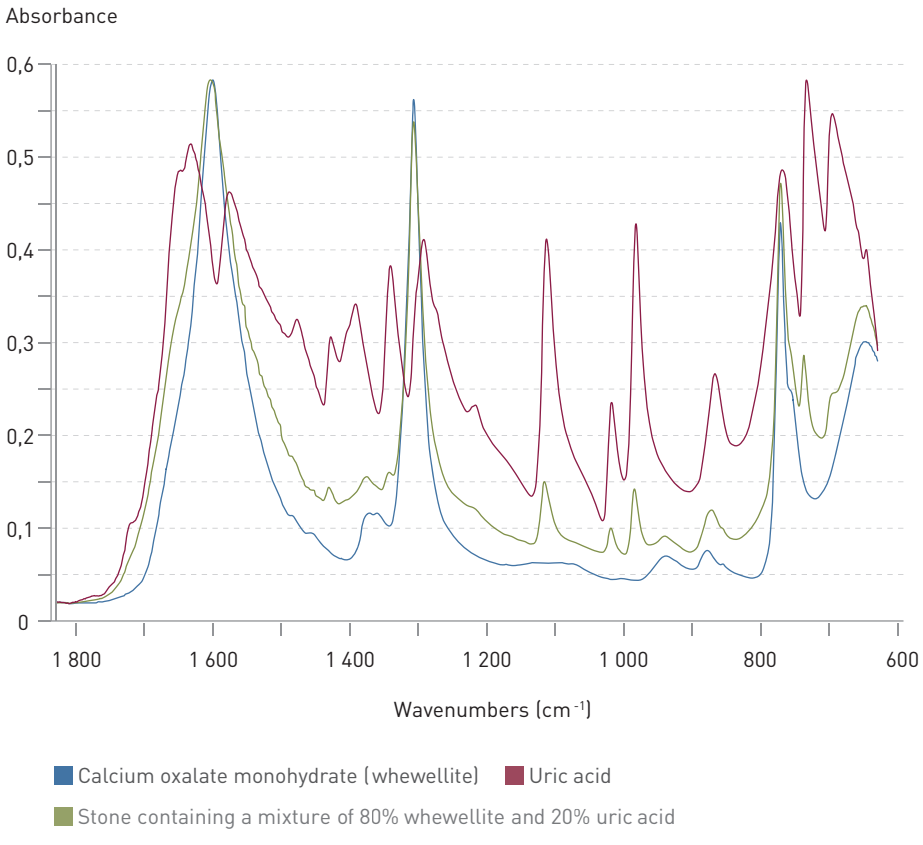

Figure 1 *Examples of infrared spectra of kidney stones. Blue: Pure calcium oxalate monohydrate (whewellite). Red: Pure uric acid. Green: Stone containing a mixture of 80 % whewellite and 20 % uric acid.*

Methods for kidney stone analysis

Infrared spectroscopy, X-ray diffraction and polarisation microscopy are internationally recommended techniques for kidney stone analysis (3, 6). Straightforward data interpretation and lower instrument costs have made infrared spectroscopy the preferred technique. In infrared spectroscopy, photons possessing energy that exactly matches the vibration energy of a covalent bond are absorbed. An infrared spectrum shows which bonds have absorbed radiation (wavelength) and the absorption efficiency (intensity). The combination of wavelengths and intensities generates a unique fingerprint for each compound, which can be used for accurate quantitative and qualitative analysis of kidney stones. Examples of infrared spectra are shown in Figure 1.

Mixed stones are common, and infrared spectroscopy can be used to determine the relative percentage content of the various components with high accuracy. Other advantages of infrared spectroscopy are rapid analysis, and reliable results even with very small amounts of sample material. Akershus University Hospital is the first hospital in Norway to use infrared spectroscopy for kidney stone analysis. Urinary calculi can be divided into groups by the main component (Table 1).

Wet chemical methods, which are still much used, only allow for the qualitative or semi-quantitative detection of a limited number of ions. Here, the stone is dissolved in a strong acid before various chemicals are added, which trigger the formation of a gas or coloured products depending on which ions are present. Crystal structures cannot be identified, which means that it is not possible to distinguish between, for example, calcium oxalate mono- and dihydrate, or different calcium phosphate compounds. Moreover, neither xanthine, 2,8-dihydroxyadenine, nor drugs can be identified.

Table 1 Common and important chemical substances and mineral components in kidney stones and their estimated frequencies.

Stone type	Chemical name	Mineral name	Chemical formula	Frequency (%)
Oxalate stones	Calcium oxalate monohydrate	Whewellite	$CaC_2O_4 \cdot H_2O$	75
	Calcium oxalate dihydrate	Weddellite	$CaC_2O_4 \cdot 2H_2O$	
Phosphate stones	Carbonate apatite	Dahllite	$Ca_{10}(PO_4)_2(CO_3)_6(OH)_2$	8
	Calcium hydrogen phosphate dihydrate	Brushite	$CaHPO_4 \cdot 2H_2O$	
	β-tricalcium phosphate	Whitlockite	$Ca_3(PO_4)_2$	
	Magnesium ammonium phosphate hexahydrate or monohydrate	Struvite Dittmarite	$MgNH_4PO_4 \cdot 6H_2O$ $MgNH_4PO_4 \cdot H_2O$	6
Uric acid and urate stones	Uric acid/uric acid dihydrate		$C_5H_4N_4O_3$ / $C_5H_4N_4O_3 \cdot 2H_2O$	
	Sodium urate monohydrate		$NaC_5H_3N_4O_3 \cdot H_2O$	10
	Ammonium urate		$NH_4C_5H_3N_4O_3$	
Metabolic stones	Cystine		$[HOOC\text{-}CH(NH_2)CH_2S]_2$	0.5–1
	Xanthine		$C_5H_4N_4O_2$	Rare
	2,8-dihydroxyadenine		$C_5H_5N_5O_2$	Rare
Drug stones	Indinavir, atazanavir, sulphonamides and others			Rare

Wet chemical methods have high error rates. For pure substances and binary mixtures, error rates of 6–94 % and 13–47 %, respectively, have been found (6). Incorrect analysis, for example not identifying infection stones or uric acid in stones, may result in inadequate therapy. Wet chemical methods are therefore considered obsolete (3, 6).

When should stone analysis be performed?

Analysis of urinary stones is recommended as a part of the basic evaluation in all first-time stone formers (3, 7) and in cases of recurrence under pharmacological prevention, early recurrence after interventional therapy with complete stone clearance and late recurrence after a long stone-free period (3). In at least 30 % of recurrences, the stone is of a different type to the first episode (8), which indicates that it might be useful to examine all recurrent stones.

In many cases, more extensive examination is required to reveal the aetiology of stone formation in the individual patient, for example 24 hour-urine measurements of calcium, oxalate and citrate (3, 7).

Conclusion

Kidney stone analysis of high quality is an essential part of the basic evaluation to identify patients at high risk of recurrent stone disease. These patients are offered extended examination. The basic evaluation, along with extended examination in selected individuals, is necessary to reveal underlying disease and to be able to offer stone-specific treatment and individualised treatment to prevent stone recurrences.

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References

1. Scales CD Jr, Smith AC, Hanley JM et al. Prevalence of kidney stones in the United States. Eur Urol, 2012; 62(1): p. 160–5.
2. Kohjimoto Y, Sasaki Y, Iguchi M et al. Association of metabolic syndrome traits and severity of kidney stones: Results from a nationwide survey on urolithiasis in Japan. Am J Kidney Dis. 2013; 61(6): 923–9.
3. Türk C, Knoll T, Petrik A et al. Guidelines on urolithiasis. European Association of Urology 2014.
4. Borghi L, Schianchi T, Meschi T et al. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. N Engl J Med 2002; 346: 77–84.
5. Karlsen SJ. Kirurgisk behandling av urolithiasis. Tidsskr Nor Lægeforen nr. 7, 2003; 938–940.
6. Hesse A, Kruse R, Geilenkeuser WJ et al. Quality control in urinary stone analysis: results of 44 ring trials (1980–2001). Clin Chem Lab Med 2005; 43(3): 298–303.
7. Osther PJ, Grenabo L, Haraldsson G et al. Metabolic evaluation and medical management of upper urinary tract stone disease. Guidelines from the Scandinavian Cooperative Group for Urinary Stones. Scand J Urol Nephrol 1999; 33: 372–381.
8. Zenga G, Zhaoa Z, Wu W et al. Interconversion of stone composition profiles from two recurrent stone episodes in stone formers. Clin Chem Lab Med 2014; 52(7): 1019–1024.

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