

# The changing composition of urinary calculi in Southern Thailand over the past 14 years

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## Abstract

**Objective:** A worldwide increased incidence of urolithiasis has been observed over the past few decades. Insight into the composition of these stones can lead to enhanced medical treatment and outcomes. The objective of this study was to examine the distribution and chemical composition of urinary calculi in Southern Thailand over the past decade.

**Materials and Methods:** An analysis was conducted on 2611 urinary calculi submitted to the Stone Analysis Laboratory, Songklanagarind Hospital, a single stone analysis laboratory in Southern Thailand. The analysis was performed from 2007 to 2020 using Fourier-transform infrared spectroscopy. The demographic results were described using descriptive statistical analyses, and the Chi-square test for trends was performed to identify changes in urinary calculi composition.

**Results:** The patients' demographic data revealed a male-to-female ratio of 2.2:1; the most common age group of affected men was 50–69 years, whereas the most common age group of affected women was 40–59 years. The most common components found in the calculi were uric acid (30.6%), mixed calcium oxalate with calcium phosphate (29.2%), and calcium oxalate (26.7%). We noted a trend of increasing uric acid calculi for 14 years ( $P = 0.00493$ ), whereas the trend for the other major components was decreasing.

**Conclusion:** The most common component of urinary calculi analyzed in Southern Thailand was uric acid, with a significant rising trend in proportion in the past decade; the trend of other major components, such as mixed calcium oxalate-calcium phosphate and calcium oxalate, decreased.

**Keywords:** Fourier-transform infrared spectroscopy, Southern Thailand, uric acid, urinary calculi, urolithiasis

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## INTRODUCTION

Urolithiasis is a common disease with varied prevalence in different regions of the world, ranging from 7% to 13% in North America, 5% to 9% in Europe, and 1% to 5% in Asia.<sup>[1,2]</sup> Its development depends on age, sex, occupation and education levels, socioeconomic status, fluid intake and dietary habits, racial distribution, and the presence of genetic

and metabolic diseases.<sup>[1,3]</sup> The incidence of urolithiasis has increased in both developed and developing countries over the past few decades.<sup>[1,2]</sup> The chemical composition of urinary calculi has been described in numerous studies from many regions globally, with calcium calculi being prevalent in all countries, whereas uric acid stones are more prevalent in countries with deserts or tropical climates.<sup>[4]</sup>

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Thailand is in South-East Asia and in the area of the “stone belt,” with a high reported rate of incidence of urolithiasis;<sup>[5]</sup> this has added to the health problems of the country and has a significant impact on its health systems.<sup>[6]</sup> By knowing the trend of calculi composition, not only we will be able to better understand how they are formed but also to indicate appropriate medical therapy; this may enable better management of this disease and may prevent its recurrence. Therefore, in this study, we aimed to identify the chemical composition of urinary calculi in South Thailand and their changing composition over a time span of 14 years; this identification could enhance the planning of urological services in future.

## MATERIALS AND METHODS

### Patient selection

The 2611 urinary calculi were collected between January 1, 2007, and December 31, 2020, using the methods of spontaneous passage, shock wave lithotripsy (SWL), endoscopic surgery, ureterorenoscopic lithotripsy, percutaneous nephrolithotomy, transurethral cystolitholapaxy, and laparoscopic or open surgery for urolithiasis were analyzed at the Stone Analysis Laboratory at Songklanagarind Hospital. We selected only the first calculi presented to the stone analysis laboratory to avoid repeated results of the same calculi (from the second or more sessions of treatment) in SWL or endoscopic surgery.

### Calculi analysis process

All calculi were analyzed in the Stone Analysis Laboratory at Songklanagarind Hospital. This is the only laboratory in Southern Thailand where calculi are analyzed, and it is therefore a fair representation of the calculi encountered in this area. The calculi were kept in plastic bags or bottles and were assigned identification numbers. All calculi were washed with sterile water to remove any contaminants, such as blood or cellular debris, and then air dried.

The first step of the analysis process is shown in Figure 1. After visual inspection and weighing, the calculi were described according to their texture and color as well as the number of calculi submitted, followed by a sampling of the surface and core. In the case of large calculi, sampling was performed at least three points from the surface area; the calculus was then broken into pieces and sampled at, at least, three points from the core area; in contrast, the small calculi were crushed into fragments to reveal their internal structure. The fragmented calculi were then mixed with potassium bromide powder, pressed into a small pellet, and analyzed through Fourier-transform infrared

spectroscopy (FTIR) using the ATI Mattson, Genesis Series, and WinFIRST programs.

### Calculi classification

The calculi were classified according to their fundamental components as follows:

- The calcium oxalate group (CaOx) was composed of calcium oxalate monohydrate (whewellite) and calcium oxalate dihydrate (weddelite)
- The calcium phosphate group (Cap) was composed of carbonate apatite (dahllite), calcium hydrogen phosphate dihydrate (brushite), amorphous calcium phosphate, tricalcium phosphate (whitlockite), magnesium ammonium phosphate (struvite), and magnesium hydrogen phosphate trihydrate (newberyite)
- The uric acid group (Ua) was composed of uric acid (uricite), uric acid dihydrate, ammonium hydrogen urate, sodium hydrogen urate, and potassium hydrogen urate
- The other groups consisted of rare calculi (such as xanthine, 2,8 dihydroxyadenine, and cystine), and mixed compositions (such as CaOx-urate or Cap-urate).

### Statistical analysis

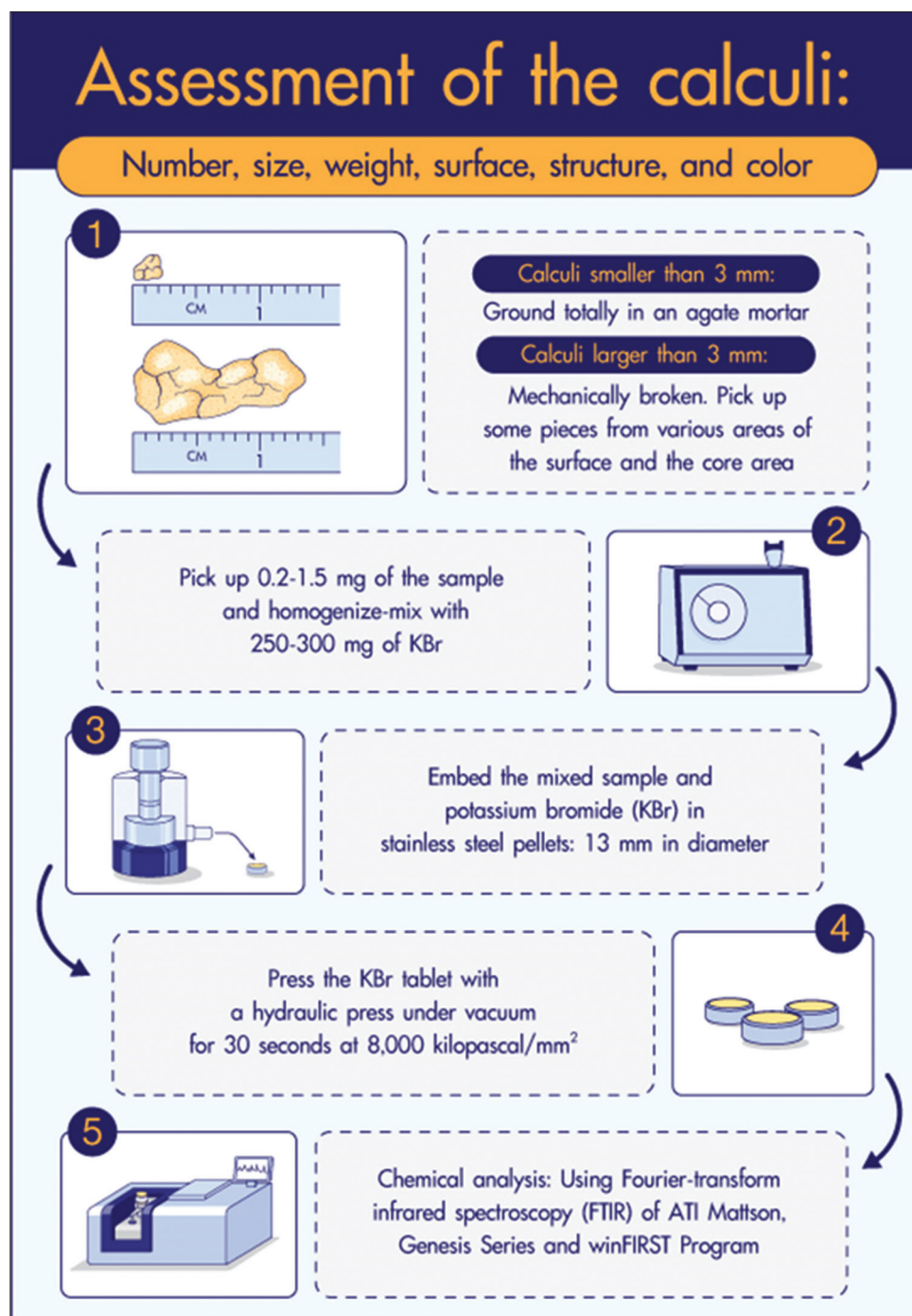
Descriptive statistics were used to present the demographic data. For an analysis of the changing trend of uric acid calculi, which is a common component in Southern Thailand, the Chi-square test was performed to identify trends in proportions. Statistical significance was set at  $P < 0.05$ . All statistical analyses were performed using the R software.

## RESULTS

The patient demographic data revealed a male-to-female ratio of 2.2:1; the most common age group was 50–59 years, whereas the second most common age group among males was 60–69 years, and the second most common age group among females was 40–49 years [Figure 2].

A total of 2611 calculi were analyzed using FTIR spectroscopy. The components most frequently encountered were uric acid (30.6%), mixed calcium oxalate with calcium phosphate (29.2%), and calcium oxalate (26.7%) [Table 1 and Figure 3]. The uric acid component increased over time, whereas the other major components decreased [Figure 4].

The proportion of uric acid was 0.4417 (range 0.3378–0.6154), as shown in Table 2, and the Chi-square for linear trend (Extended Mantel–Haenszel: 7.90459)



**Figure 1:** Calculi analysis process

was significant ( $P = 0.00493$ ). The scatter plot of category proportions with a regression line is shown in Figure 5.

## DISCUSSION

This study presents the composition of 2611 urinary calculi collected in Southern Thailand over 14 years, analyzed using FTIR. The results revealed that the most common component of urinary calculi was uric acid, with a significant rising trend in proportion, whereas the other major components were

mixed calcium oxalate, calcium phosphate, and other rare components. The demographic data revealed that calculi were 2.2 times more common in men than in women. The most common age group of urolithiasis patients was 50–59 years, and the second most common occurrence was in older males (50–59 years) and in younger females (40–49 years).

The beginning of urolithiasis prevalence studies in Thailand dates to 1961, with a reported prevalence of 17.7/100,000,

**Table 1: Chemical composition of the urinary calculi (n=2611)**

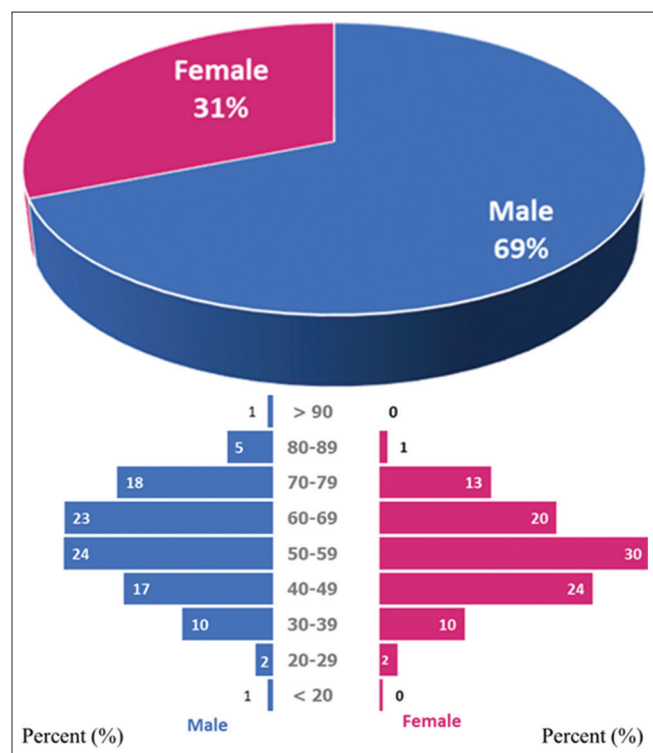
| Component | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|-----------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| CaOx      | 40   | 56   | 82   | 81   | 51   | 71   | 69   | 47   | 47   | 30   | 29   | 29   | 23   | 40   |
| CaOx-Cap  | 46   | 33   | 96   | 110  | 65   | 71   | 64   | 62   | 51   | 42   | 32   | 32   | 20   | 38   |
| Ua        | 45   | 51   | 69   | 76   | 64   | 84   | 58   | 55   | 71   | 43   | 49   | 39   | 40   | 56   |
| Other     | 15   | 17   | 23   | 34   | 31   | 34   | 36   | 24   | 32   | 20   | 22   | 13   | 22   | 30   |
| Total     | 146  | 157  | 270  | 301  | 211  | 260  | 227  | 188  | 201  | 135  | 132  | 113  | 105  | 165  |

CaOx: Calcium oxalate component, CaOx-Cap: Mixed calcium oxalate-calcium phosphate, Ua: Uric acid component

**Table 2: Proportion of the calculi containing uric acid**

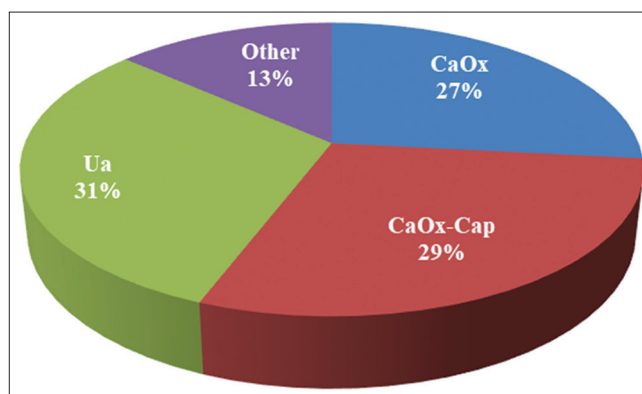
| Year  | Calculi containing uric acid | Calculi containing nonuric acid | Total | Proportion of calculi containing uric acid | OR        |
|-------|------------------------------|---------------------------------|-------|--|-----------|
| 2007  | 45                           | 101                             | 146   | 0.4455                                     | Reference |
| 2008  | 51                           | 106                             | 157   | 0.4811                                     | 1.0800    |
| 2009  | 69                           | 201                             | 270   | 0.3433                                     | 0.7700    |
| 2010  | 76                           | 225                             | 301   | 0.3378                                     | 0.7580    |
| 2011  | 64                           | 147                             | 211   | 0.4354                                     | 0.9770    |
| 2012  | 84                           | 176                             | 260   | 0.4773                                     | 1.0710    |
| 2013  | 58                           | 169                             | 227   | 0.3432                                     | 0.7700    |
| 2014  | 55                           | 133                             | 188   | 0.4135                                     | 0.9280    |
| 2015  | 71                           | 130                             | 201   | 0.5462                                     | 1.2260    |
| 2016  | 43                           | 92                              | 135   | 0.4674                                     | 1.0490    |
| 2017  | 49                           | 83                              | 132   | 0.5904                                     | 1.3250    |
| 2018  | 39                           | 74                              | 113   | 0.5270                                     | 1.1830    |
| 2019  | 40                           | 65                              | 105   | 0.6154                                     | 1.3810    |
| 2020  | 56                           | 109                             | 165   | 0.5138                                     | 1.1530    |
| Total | 559                          | 1178                            | 1737  | 0.4417                                     | -         |

OR: Odds ratio



**Figure 2:** Demographic data of patients with calculi in Southern Thailand (n = 2611) and page 1 Left column line 24; lithotripsy (SWL), endoscopic surgery: ureterorenoscopy

which increased to 183.8/100,000 in the year 2005;<sup>[7-9]</sup> this had a significant impact on health systems due to the cost of diagnosis and treatment, as well as the loss of working hours due to the disease.<sup>[10]</sup> This led to the development of

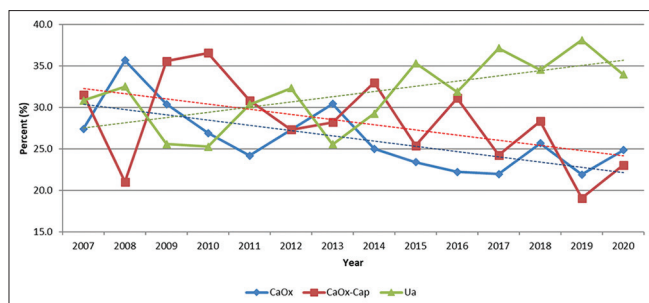


**Figure 3:** The major components of urinary calculi in Southern Thailand

community treatment programs, resulting in a decreased prevalence of 90.75/100,000 people in 2018.<sup>[5]</sup> The same situation was noted in Malaysia, Thailand’s neighbor, which reported a prevalence of 33.3/100,000 in 1981 that increased to 224.2–442.7/100,000 in 1990 and later decreased to 9.8–37/100,000 in 2013.<sup>[11-13]</sup> However, the prevalence of urolithiasis has increased in other parts of Asia (including China, Japan, and India) and the Middle East (including Saudi Arabia, Kuwait, Iran, and Israel).<sup>[2]</sup>

It is documented that urolithiasis occurs more commonly in males than in females, which is also confirmed by our results: the male-to-female ratio in this study was 2.2:1. This result was the same mentioned in early epidemiologic studies, which showed that the ratio of urinary calculi



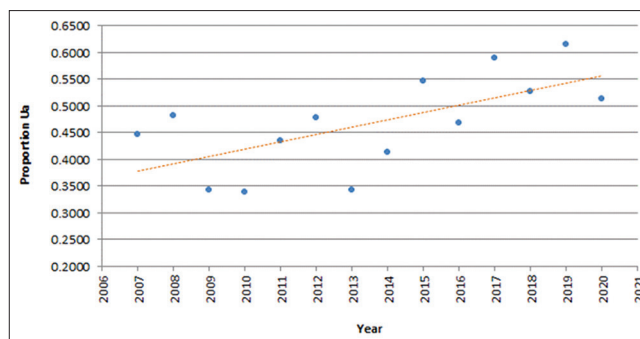


**Figure 4:** Trends of the major components in urinary calculi in Southern Thailand. CaOx: Calcium oxalate component, CaOx-Cap: Mixed calcium oxalate-calcium phosphate, Ua: Uric acid component

in males was 2.2–3.4 times that in females.<sup>[14]</sup> The most common age group of urolithiasis patients in this study was 40–59 years, which is the same age group mentioned in previous reports from Thailand;<sup>[7,9,15]</sup> however, it is younger in comparison to reports from Western countries, where the most common age group was 60–70 years.<sup>[16]</sup>

The chemical composition of urinary calculi provides valuable information, as stated by the American Urological Association guidelines on the medical management of kidney calculi, recommended for stone analysis to classify patients and guide prevention.<sup>[17]</sup> Thus, the chemical composition of calculi has been reported worldwide, showing that calcium calculi are prevalent in all countries; however, the prevalence of uric acid calculi is higher in countries with deserts or tropical climates. Our data from Southern Thailand reported a high incidence of uric acid calculi, i.e. 30.6%. The uric acid composition in the United States was 14.3%,<sup>[16]</sup> whereas those in European countries were highly variable: Germany 17%–25%, Sweden 4%,<sup>[18,19]</sup> and Norway 8.9%.<sup>[20]</sup> Reports of uric acid calculi in Asian and Middle Eastern countries also displayed a wide variation, such as in Israel, which reported a prevalence of up to 40%;<sup>[19]</sup> Saudi Arabia, 19%; Iran, 16.2%; Japan, 5.3%;<sup>[6]</sup> and China, 5.9%–6.9%.<sup>[21]</sup> The high incidence of uric acid calculi may be associated with differences in dietary habits and living standards, ranging from urbanized to industrialized, which result in changes in the patients' nutritional status and the increased occurrence of metabolic syndrome.<sup>[7]</sup> Together with the warmer weather, the effect of insensible water loss increases urinary supersaturation<sup>[18]</sup> and affects the composition of urinary calculi.

The incidence of uric acid calculi also increased over time; our data revealed a significant rising trend in the proportion of uric acid (similarly to the report from Japan), from 4.6% in 1965 to 5.3% in 2005; the incidence in Algeria was 6.2% in 1990 and increased to 8.8% in 2006.<sup>[6]</sup> A report from China revealed no increase in the uric acid composition during 13 years of observation.<sup>[21]</sup>



**Figure 5:** Scatter plot of the proportions of uric acid (Ua) with a regression line ( $P = 0.00493$ ). Ua: Uric acid component

The formation of uric acid calculi depends on low urine output and high urine uric acid levels, with the most important associated factor being low urinary pH.<sup>[22]</sup> Therefore, the crystallization process of uric acid calculi can be reversed by the alkalization of urine, allowing oral chemolysis as an alternative therapy to surgical intervention. Following the European Association of Urology Guidelines Panel, the urine pH should be adjusted to 6.5–7.2. Alkaline citrate and sodium bicarbonate can be used as oral alkalinizing agents.<sup>[23]</sup> However, uric acid calculi can be prevented by liberal fluid intake to increase urine volume and alkalinizing measures to raise the urine pH to 6.5. Finally, dietary modifications are recommended, although there is insufficient evidence of their efficacy in the prevention of uric acid calculi.

Inevitably, this study has several potential limitations. For instance, the reported data may not reflect the real prevalence of calculi in Southern Thailand, because the calculi submitted for analysis were from hospitals with urologists; therefore, we could have missed calculi that were treated in other hospitals. Despite this limitation, the present study has value as it is one of the very few studies to provide longitudinal information on the changes in the composition of urinary calculi over a time frame of 14 years, and the rising trend of uric acid calculi in Southern Thailand. Further studies are needed to determine the factors associated with uric acid calculi so that the recurrence of calculi in future is prevented.

## CONCLUSION

The results of the present study revealed that the most common component of urinary calculi in Southern Thailand was uric acid, with a significant rising trend in proportions over the past decade. The trend of the other major components of urinary calculi, such as mixed calcium oxalate-calcium phosphate and calcium oxalate, decreased.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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