

## MINERALOGY OF PANCREATIC CALCULI

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### ABSTRACT

Pancreatic calculi from patients with chronic pancreatic disorders from the Mexico City area are 75% calcitic stones, with an average weight of 1.30 g and ranging in size from 7 to 28 mm, and 25% organic stones, with an average weight of 0.11 g and ranging in size from 4 to 12 mm. The calcitic calculi contain calcite phenocrysts carrying Si, S, and P; anhedral calcite crystallites, some with pseudo-hexagonal morphology; and irregular crystals containing Si and Ca+Si, on a (Ca+Si)-containing organic matrix that represents about 20% volume of the calcitic stone. The organic calculi have a few crystallites of calcite dispersed in an organic matrix that contains small amounts of Si, P, I, S, and Cl. Their infrared analyses indicate that whereas the calcitic stones present the characteristic vibrations of calcite, OH<sup>-</sup> stretching, Si-O-Si stretching, and organic components, the organic stones are characterized by OH<sup>-</sup> stretching at lower wavelengths and by intense vibrations at 1,650, 1,520, 1,385, and 1,230 cm<sup>-1</sup> and others presumably representing the organic phase. The crystallization of Si- and (Si+Ca)-containing phases is attributed to possible dystrophic mineralization events such as rheumatoid arthritis and urolithiasis. The two types of calculi may represent distinct pathogenesis, formation from different fluids or from a common fluid with dissimilar concentrations of suppressors of CaCO<sub>3</sub> crystallization, or in response to divergent reactions.

Key words: Geochemistry, mineralogy, pancreatic calculi.

### RÉSUMEN

Los cálculos pancreáticos de pacientes con enfermedades crónicas del páncreas en la ciudad de México consisten en piedras calcíticas en un 75%, con un peso promedio de 1.30 g y un tamaño de entre 7 y 28 mm, y en piedras orgánicas en un 25%, con un peso promedio de 0.11 g y un tamaño de entre 4 y 12 mm. Los cálculos calcíticos contienen fenocristales de calcita que contiene Si, S y P; cristallitos anedrales de calcita, algunos con morfología pseudo-hexagonal; y cristales irregulares que contienen Si y Ca+Si, en una matriz orgánica que contiene Ca + Si y que representa cerca de 20% en volumen de la piedra calcítica. Los cálculos orgánicos tienen unos cuantos cristallitos de calcita dispersos en una matriz orgánica que contiene cantidades pequeñas de Si, P, I, S y Cl. Sus espectros de análisis infrarrojo indican que mientras que los cálculos calcíticos presentan las vibraciones características de la calcita, alargamientos OH<sup>-</sup> y Si-O-Si, y componentes orgánicos, los cálculos orgánicos están caracterizados por alargamiento OH<sup>-</sup> de longitudes de onda menores y por vibraciones intensas a 1,650, 1,520, 1,385 y 1,230 cm<sup>-1</sup> y otras que presumiblemente representan la fase orgánica. La cristalización de las fases que contienen Si y Si+Ca se atribuye a posibles eventos de mineralización distrófica, como artritis reumatoide y urolitiasis. Los dos tipos de cálculos pueden representar patogénesis diferentes, originadas a partir de fluidos diversos o de un fluido común con concentraciones distintas de supresores de cristalización de CaCO<sub>3</sub>, o en respuesta a reacciones divergentes.

Palabras clave: Geoquímica, mineralogía, cálculos pancreáticos.

### INTRODUCTION

Pancreatic stones are uncommon calculi and their mineralogy and mode of formation are rarely reported. The cases studied have been on material from India or, infrequently, from other Asian and African locations where pancreatic disorders occur, often in endemic proportions. They form in patients with chronic pancreatic disorders and are associated with nutritional, hereditary, idiopathic, hypercalcemia, and alcoholic origins; the most common nutritional or tropical pancreatic ailments have been observed in children and young

adult populations of developing nations (Zuidema, 1959; Payan *et al.*, 1972; Pitchumoni, 1973; Pitchumoni, 1984). The stones are composed of calcite, with occasional vaterite, aragonite, and rarely with hydroxyapatite, and they have an organic matrix that includes proteins, glycosaminoglycans, and cellular elements (Eliason and Wetty, 1948; Edmondson *et al.*, 1950; Lagergren, 1962; Mallet-Guy *et al.*, 1969; Gibson, 1974; De Caro *et al.*, 1979; Multigner *et al.*, 1983; De Caro *et al.*, 1984; Giorgi *et al.*, 1985; Bockman *et al.*, 1986; Montalto *et al.*, 1986; Schultz *et al.*, 1986). The calcite is microcrystalline, of a habit that has been associated with the inhibiting effects of the organic components of the stone or of the pancreatic juice that suppresses the crystallization of CaCO<sub>3</sub> from the pancreatic solutions that are normally supersaturated with CaCO<sub>3</sub> (Harada *et al.*, 1982, 1983; Multigner *et al.*, 1983; Montalto *et al.*,

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1988). The organic matrix has been characterized by several authors (Matsuhiro and Nemoto, 1968; Harada *et al.*, 1980; Multigner *et al.*, 1983; De Caro *et al.*, 1985; Bockman *et al.*, 1986; Montalto *et al.*, 1988).

Pancreatic calculi have not been investigated in patients from Mexico, basically because pancreatic disorders are not common in the country. We undertook the present investigation to study the mineralogy and pathogenesis of pancreatic lithiasis from local patients and the relation of the stones with those from other locations, with particular emphasis on their inorganic mineral components.

#### EXPERIMENTAL WORK

Twelve pancreatic stones removed surgically from patients treated in a major hospital located in the Mexico City area were studied. The stones were collected over a period of 10 years and kept in alcohol. For the present study, they were weighted, measured, and examined megascopically with a simple, low-magnification binocular microscope. The samples were then sectioned, fractured, or finely ground for analysis. No chemical treatment was applied to remove any extraneous material.

The inorganic components were studied by optical microscopy using thin sections and index-oil immersion methods on crushed fragments, using a Zeiss petrographic microscope provided with polarized transmitted- and reflected-light. X-ray diffraction analysis (XRD) of randomly oriented powders was used for their identification, using a Siemens D5000 diffractometer equipped with filtered  $\text{CuK}\alpha$  radiation with the goniometer set at  $2\theta$  angles from  $5^\circ$  to  $70^\circ$  at a speed of  $1^\circ 2\theta/\text{min}$ . Infrared absorption spectrometry (IR) was applied to investigate the inorganic and organic components, using a Perkin-Elmer 783 double-beam spectrometer operated at a scanning speed of  $1,000 \text{ cm}^{-1}/\text{min}$  from  $4,000 \text{ cm}^{-1}$  to  $2,000$  and at  $500 \text{ cm}^{-1}/\text{min}$  between  $2,000 \text{ cm}^{-1}$  and  $200$  wavenumbers, on material dried and pressed into KBr discs. Microtextural relations, crystallization, and morphology of the calculi were interpreted in gold- and graphite-covered, broken, flat, unpolished surfaces using a JEOL scanning electron microscope (SEM) coupled to a Kevex energy-dispersive spectrometer (EDS) with Be-window detector. The identification of the mineral components was straightforward in some cases, whereas other components contained in low concentrations not detected by XRD were identified from the qualitative element detected by EDS on fragments selected by SEM and from the IR spectra. Quantitative EDS analysis was not attempted given the size of the specimens, the non-flat surface, and the lack of proper reference materials.

#### RESULTS AND DISCUSSION

Initial classification of the pancreatic stones is based on their megascopic characteristics (Table 1). Of the 12 samples

Table 1. Megascopic characteristics of pancreatic stones.

	Calcitic	Organic
Fracture	Uneven	Conchoidal
Hardness	Medium hard	Medium soft
Colour	White yellow	Amber
Lustre	Resinous, dull	Resinous
Diaphaneity	Opaque	Translucent
Surface	Knobbed, relieved	Smooth
Texture	Botryoidal, concretionary	Glassy
Columnar		
Size ( $\mu\text{m}$ )	7-28	4-12
Weight (g)	0.11-7.16	0.02-0.23
Abundance (%)	75	25

examined, 75% is comprised of white calcitic stones with yellowish to greenish tints, that are irregular, relatively hard, light, and porous, with resinous dull luster and a knobbed surface relieved by crystals, often in botryoidal, reniform, concretionary, and columnar aggregates up to 3 mm in size. These calcitic stones show in thin sections a lumpy microtexture, with predominant subhedral to anhedral crystallites of calcite forming orbicular arrangements with abundant internal voids, in a non-crystalline, organic matrix that represents about 20% of the volume; also present are some unidentified, black, circular, opaque spots.

X-ray diffraction indicates well-crystallized calcite as the main mineral component. Other forms of  $\text{CaCO}_3$  such as vaterite or aragonite, that have been reported in pancreatic stones from other localities (Schultz *et al.*, 1986), are not confirmed in the present study. Studies by SEM document the presence of calcite in the forms of: (1) reniform concretionary aggregates with a knobby surface (Figure 1, a); (2) parallel lamellar aggregates (Figure 1, b); (3) large subhedral crystals (Figure 1, c); (4) and anhedral to subhedral crystallites less than  $10 \mu\text{m}$  in size (Figure 1, d). Also present, there are opal (Figure 1, e and f), a few large subhedral crystals containing minor Si, S, and P (Figure 1, f), and corroded crystals containing Ca+Si in about equal proportions, possibly representing some form of calcium silicate (Figure 1, f).

The organic matrix of the calcitic stones represents about 20% by volume. It is compact, uniform, and separated from calcite (Figure 2, a). In other calculi, the organic matrix abounds in vacuoles (Figure 2, b). In others appear pockets filled with a second darker, cracked, organic phase containing minor concentrations of Si, distributed in another organic phase that does not contain any Si (Figure 2, c). In a fourth type, long, thin ribbons free of inorganic components rest on the matrix (Figure 2, d). Their nature is hard to elucidate because of the long storage of the specimens but one ventured

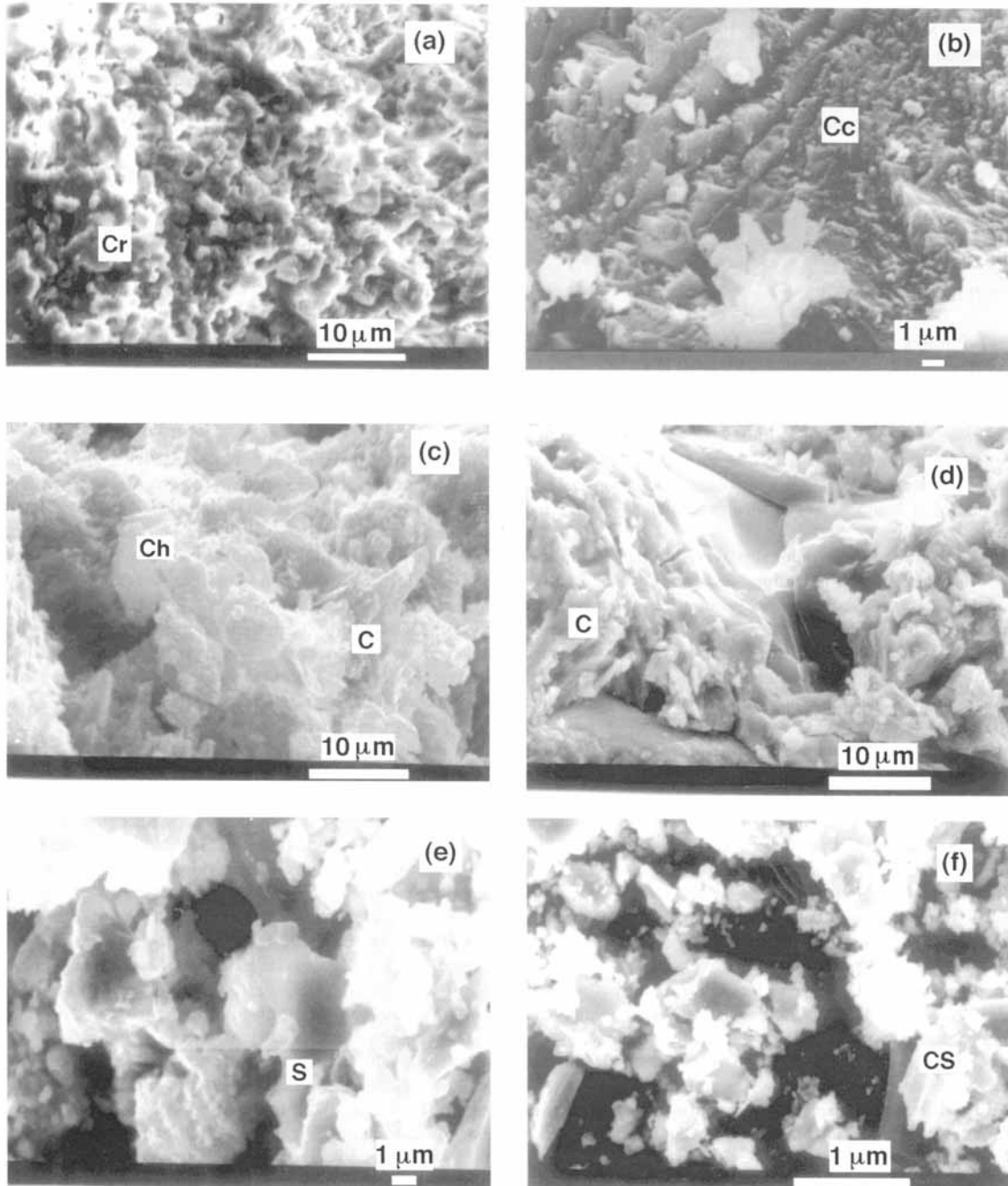


Figure 1. Scanning electron micrographs of pancreatic calcitic calculi showing typical: *a*, reniform concretionary aggregation of calcite; *b*, columnar aggregation of calcite; *c*, calcite crystals, some displaying pseudohexagonal morphology; *d*, calcite crystallites less than 10  $\mu\text{m}$  in size; *e*, calcite and opal; *f*, calcite, opal, and calcium silicate hydrate. Cr: calcite reniform; Cc: calcite columnar; C: calcite; Ch: pseudohexagonal calcite; S: opal; CS: calcium silicate.

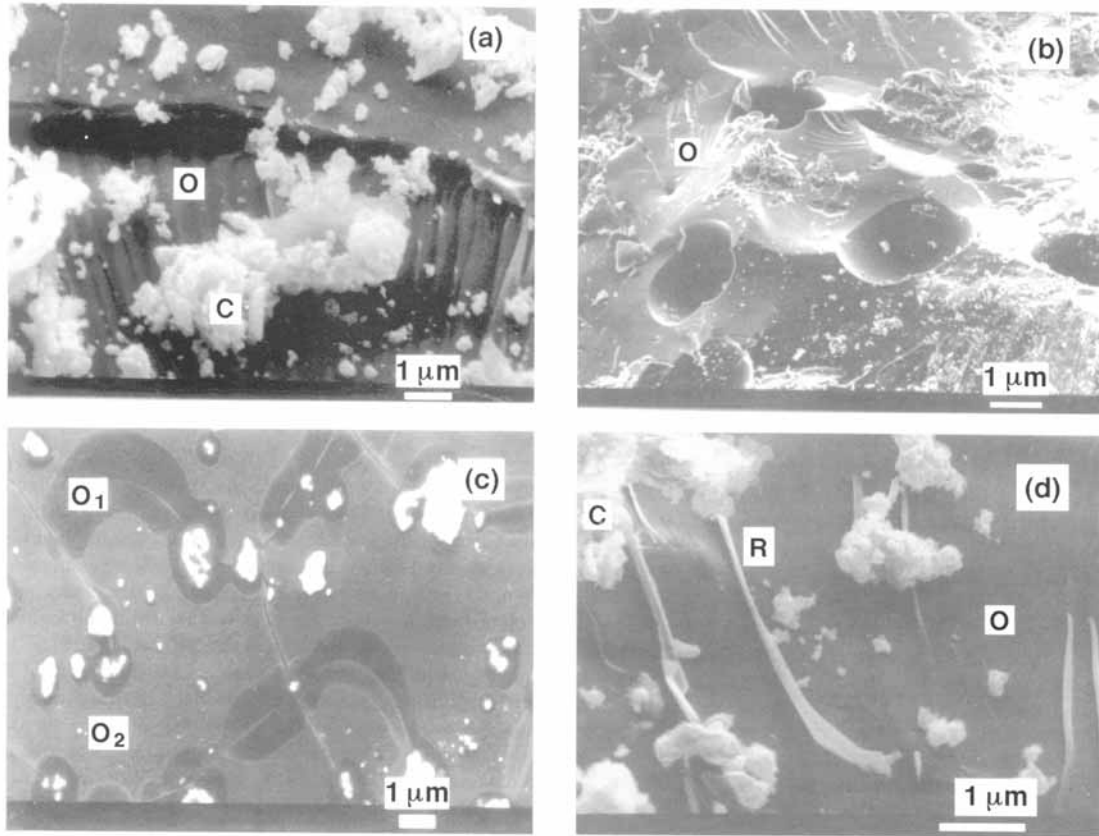


Figure 2. Scanning electron micrographs of calcitic stones showing the organic matrix: *a*, compact lamellae; *b*, matrix with abundant vacuoles; *c*, matrices of different compositions; *d*, organic ribbons of possible proteins resting on the organic matrix. C: calcite, O<sub>1</sub>: organic matrix; O<sub>2</sub>: organic matrix; R: organic ribbons.

interpretation is that they could correspond to the fibrillated glycosaminoglycans or glycoproteins reported from transmission electron microscopic studies (Harada *et al.*, 1983; Bockman *et al.*, 1986). The largest component of the organic phase has been reported to be a protein of molecular weight 14,000 that inhibits the precipitation of CaCO<sub>3</sub> (Montalto *et al.*, 1988). Infrared absorption studies on the calcitic stones confirm calcite as their main mineral constituent, characterized by vibrations at 1,785; 1,425; 872, and 320 cm<sup>-1</sup> (Table 2, Figure 3). Broad weak and medium intense absorption bands respectively at 1,160 and 1,050 cm<sup>-1</sup> are in the range of the intense asymmetric Si-O-Si stretching vibration and confirm the existence of opal or silicate phases, coincident with the SEM studies. The IR spectra indicate different stages of hydroxylation and absorption bands comparable to those reported for quartz and the mineral calcium silicates. A medium intense broad absorption at 1,630 cm<sup>-1</sup> represents the organic matrix. Aragonite reported for other calculi was not

detected (Farmer, 1974; Scheetz and White, 1977; Povarennykh, 1978; Bischoff *et al.*, 1985; Salisbury *et al.*, 1991).

The second group of pancreatic stones is represented by three organic calculi, 25% of the total population, that are brown to black, with yellow and amber tints, translucent, irregular, and softer than the calcitic calculi, with a resinous luster, smooth surface, and no apparent mineral or inorganic components. Under polarized light, the predominant phase is brown and non-crystalline, with few crystallites of calcite. XRD indicates that the calculi are essentially non-crystalline with only weak reflections from calcite. SEM studies show very minor calcite, less than 2% by volume, distributed over the organic matrix (Figure 4). EDS on material selected by SEM shows minor I, S, Cl, Si, and P for this non-crystalline organic matrix; the few dispersed crystallites of calcite contain minor Si, P, S, Cl, and I, and traces of K. Infrared analyses of these organic stones indicate more intense, larger and broader OH<sup>-</sup> stretching vibrations than those in the

Table 2. Infrared vibrations of pancreatic calcitic and organic stones.

Calcitic		Organic	
$\lambda$ (cm <sup>-1</sup> )	Assignment	$\lambda$ (cm <sup>-1</sup> )	Assignment
3,400	OH-stretching	3,270	OH-stretching
		3,020	
2,920		2,940	
2,904	OH <sub>2</sub> -stretching	2,904	OH <sub>2</sub> -stretching
2,835		2,850	
2,500			
1,785	$\nu_2$ calcite (out-of-plane bend)		
1,630	Organic	1,650	Organic
		1,520	Organic
1,425	$\nu_3$ calcite (antisymmetric stretching)	1,440	Organic
		1,385	Organic
		1,340	Organic
		1,280	Organic
		1,230	Organic
1,160	Si-O-Si stretching	1,160	Organic
		1,070	Organic
1,050	$\nu_1$ calcite (symmetric stretching) Si-O-Si stretching	1,060	Organic
		925	Organic
		828	Organic
872	$\nu_2$ calcite (out-of-plane bend)		
		745	Organic
710			Organic
		700	Organic
		600	Organic
320	$\nu_4$ calcite (external libration)		

calcitic stones, occurring at the higher frequency of 3,270 cm<sup>-1</sup> that suggests association with lighter atoms. The organic phase is characterized by intense broad vibrations at 1,650, 1,520, and 1,385 cm<sup>-1</sup> (Table 2, Figure 3).

The evidence presented indicates that pancreatic calculi are either calcitic or organic with clear, well-defined differences. Calcitic calculi are composed largely of calcite whereas the organic calculi hardly contain any calcite. Calcite is either pure, carries minor Si and P, or contains Si, P, and S in higher concentrations; it occurs as large crystals or as

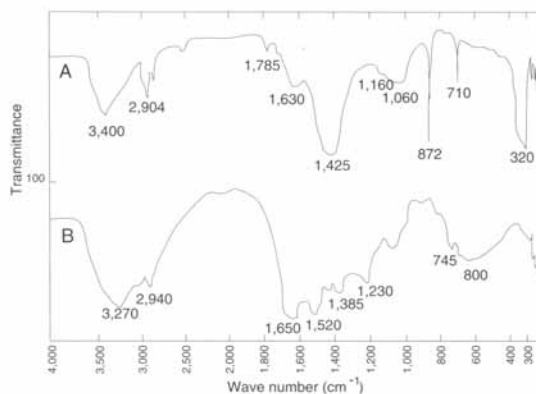


Figure 3. Infrared absorption spectra of calcitic (A) and organic (B) pancreatic calculi.

crystallites. Associated inorganic phases are opal and hydrated calcium silicate. They support the possibility that their crystallization could be from predominantly calcitic fluids or from saturated CaCO<sub>3</sub> pancreatic juices containing the minor Si and P also identified in the organic matrix. Associated crystallites of calcite could originate from subsequent crystallization events or calcitic fluids. The composition of the calcitic calculi confirms the known normal association of Si with calcitic inorganic concretions and in dystrophic mineralization events such as rheumatoid arthritis and urolithiasis. In the organic calculi, the very minor content of calcite and the traces of Si, P, I, S, and Cl in the organic matrix, suggest deposition from pancreatic fluids undersaturated in or essentially devoid of CaCO<sub>3</sub>, distinct from the fluids associated with the calcitic calculi. The formation of either type of calculus may be dependent on the nature of the pancreatic fluids, which may be of two different compositions

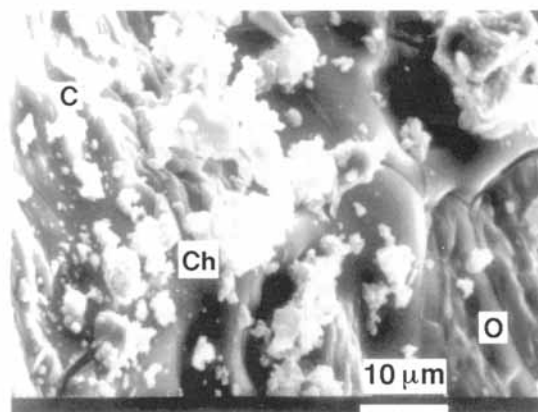


Figure 4. Scanning electron micrograph of organic pancreatic calculi showing minor crystallites of calcite (C) and pseudohexagonal calcite (Ch), containing Si, P, Cl, and I, on the organic matrix (O) that has I, Cl, P, S, and Si.

or, if of the same composition, those associated with the organic calculi must have high concentrations of suppressors of  $\text{CaCO}_3$  crystallization. Mild dissolution or substitution for calcium in calcite by other elements, mainly Mg, by increasing Mg uptake in patients, as has been suggested for other dystrophic mineralization events (urolithiasis), could assist in the treatment of the disease.

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