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ORIGINAL PAPER

Urine alkalinization for dissolution of uric acid stones and treatment of other urological diseases with a treatment combining potassium magnesium citrate and theobromine

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Abstracts were presented at 1st-2nd-3rd-4th-5th Edition of the Clinical Cases Contest related to the non-surgical clinical management of renal lithiasis. Full texts are available at https://professional.devicare.com/concurso-casos/en/

Summary ***Background: Urine alkalinization can be used for the treatment of some urological diseases. Methods: A series of cases showing the beneficial effects of urine alkalinization with combination of potassium magnesium citrate and theobromine for the dissolution of uric acid stones and the treatment of other urological pathological conditions is presented.***

Results: Alkalinization was effective in the dissolution of uric acid renal stones in various clinical conditions. Two cases of bilateral renal stone, four cases of staghorn renal stone, seven patients with unilateral renal stone, and five cases of ureteral stone were described. In this group the age ranged from 46 to 91 years, the M/F ratio was 7/11, the density of the stones ranged between 300 and 528. In most cases the urinary pH ranged from 5 to 5.5. Diabetes was observed in 4 cases, obesity in 4 cases and hyperuricemia in 7. Alkalinizing treatment achieved complete dissolution of the stone in 12 cases and almost complete or partial dissolution in other 6. A combination of potassium magnesium citrate and theobromine was used in all the cases. In 4 cases the administration of allopurinol was associated. In one case with obstructive ureteral stones, stone dissolution was obtained with the combined administration of bicarbonate via nephrostomy and intravenous bicarbonate and oral treatment with citrates. Stone dissolution of uric acid stones has also been described in some specific clinical conditions such as Crohn's disease with ileostomy, outcome of partial nephrectomy, cross-fused renal ectopia. Alkalinization was also used to prevent encrustation of a self-expanding metallic ureteral stent. Alkalinization has also been employed during the period of Mitomycin administration for the treatment of non-muscle infiltrating bladder tumors and for the treatment of overactive bladder.

Conclusions: The findings of these case reports demonstrate that urinary alkalinization with frequent monitoring of urinary pH can be successfully employed in the non-surgical treatment of uric acid stones of different sizes in various locations.

KEY WORDS: Urinary calculi; Uric acid; Alkalinization; Potassium; Magnesium; Citrate; Theobromine.

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Introduction

The physiological value of urinary pH varies between 4.5 and 8.0, although the urine pH over 24 hours usually ranges between 5.7 and 6.3 so minimizing the risk of pH-dependent crystal formation (1). Urinary pH depends on dietary intake, metabolism and post-renal urinary changes due to infection by some bacterial species. Urinary pH values lower than 5.5 cause the formation of crystals or stones of uric acid which are poorly soluble in acidic urine. For this reason, products based on bicarbonate or citrate have long been used for the treatment and prevention of uric acid stones (2, 3). However, excessive alkalinization can increase the value of urinary pH above a threshold beyond which the precipitation of sodium urate and especially phosphate salts are favored. The target value of urinary pH for the dissolution of uric acid stones is between 6 and 6.5 and it must be carefully monitored (4, 5). The concomitant administration of theobromine, which has a pH-independent solubilizing action on uric acid crystals, may be useful to avoid excessive alkalinization (6, 7).

Alkalizers are also effective in dissolving crystals and stones consisting of certain drugs such as sulphadiazine. Urine alkalinization has also found application in the treatment of other urological diseases. Alkalizers are used for the symptomatic treatment of uncomplicated urinary tract infections in some countries (8), although the efficacy of this treatment has not been confirmed by randomized trials. The administration of alkalizing agents has also been proposed for the treatment of urinary frequency and pain in patients with interstitial cystitis because afferent C-fibers in the bladder wall could be activated by H+ ions frum acidic urine (9, 10).

Finally, urine alkalinization has been associated with intravesical Mitomycin treatment of non-muscle infiltrating bladder tumors to stabilize the drug and increase its absorption into the bladder wall (11).

Case series

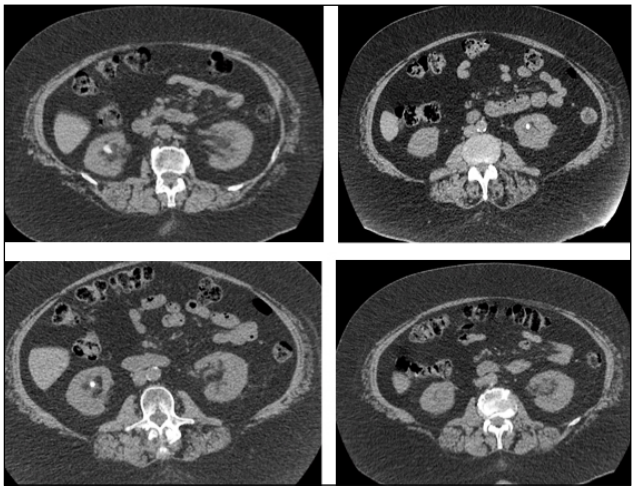
Bilateral renal stone (Table 1)
Lit-Control® pH Up as a great alternative for uric acid stones (María Belén Alonso - 2nd Ed. 2021)

We report the case of a 71-year-old obese woman diagnosed with bilateral uric acid lithiasis who required urgent urinary referral, after which alkalinising treatment with potassium citrate was prescribed without benefit. The patient had to undergo percutaneous nephrolitectomy, a procedure which failed to remove all the kidney stones. After this, the patient was treated with *Lit-Control® pH Up*, achieving almost a total resolution of her kidney stones (Figure 1).

Table 1.
Bilateral renal uric acid stones.

RENAL BILATERAL STONES (N = 2)					
Author	**Patient & Stone**	**HU**	**Treatment**	**Outcome**	**Metabolic**
María Belén Alonso 2021	71 yrs F Bilateral stones Obstructive left stone 23.6 mm	528	K citrate 10 mEq x 3 (no benefit) + DJ stent PCNL failure Lit-Control® pH Up x 2 + bicarbonate Right DJ stent	3 months complete left stone dissolution decreased size of right stone	Obesity Dyslipidemia Ur pH 5.5
Alberto López 2023	73 yrs F Right kidney 9 mm UPJ stone+ calyceal stones + partial coralliform of pelvis and lower calix Left kidney non-ostructive stone		Lit-Control® pH Up x 3	4 months Residual stone in right lower calix. Microliths in left middle and lower calyces 8 months No stones	Diabetes Obesity sCr 3.61 at admission Ur pH 5.5
Lit-Control® pH Up: Potassium citrate 200 mg, Magnesium Citrate 200 mg, Theobromine 60 mg.					

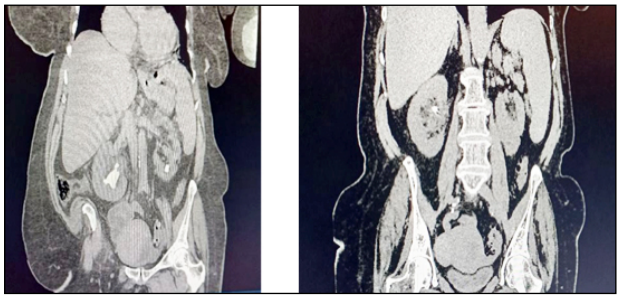
Figure 1.
Kidney stone in the lower calyx of the left kidney and a kidney stone in the right kidney before and after treatment.



Effective alkalinizing chemolysis in multiple uric acid nephrolithiasis and coralliform calculi (Alberto López - 4th Ed. 2023)

A 73-year-old diabetic woman with high cardiovascular morbidity was referred to the emergency department with clinical and laboratory findings of urinary sepsis. Urinalysis showed urinary pH 5 and abundant amorphous urates in the sediment. The CT scan showed multiple bilateral nephrolithiasis and a large pseudo-coralliform stone in the right kidney, causing ipsilateral obstructive uropathy. Urgent placement of a double J catheter

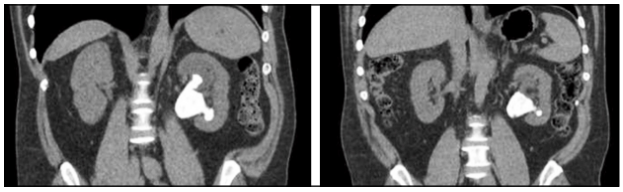
Figure 2.
Dissolution of almost all multiple bilateral renal stone including a large pseudo-coralliform stone in the right kidney after 4 months of alkalinizing treatment with Lit-Control® pH Up.



and admission to the intensive care unit was performed. Once the septic process was concluded, she was reviewed in consultation and alkalinizing treatment with *Lit-Control® pH Up* was decided. After four months, she presented a satisfactory evolution, good tolerance to treatment, and dissolution of almost all uric acid lithiasis. Subsequent control showed normal renal ultrasound, and the metabolic study showed normal uric acid and citrate excretion in urine, as well as improvement of renal function and urinary pH with a current value of 6 (Figure 2).

Staghorn renal stones (Table 2)
Combined medical approach for uric acid staghorn lithiasis (Laura Sánchez - 1st Ed. 2020)
Medical treatment for uric acid lithiasis comprises two modalities: stone formation prevention and chemolysis with curative intent. The Authors present the results of the combined medical treatment of uric acid lithiasis for the purpose of stone size reduction. The case of a 54-year-old man was presented who, after an episode of mild, self-limited hematuria, was diagnosed by CT scan with staghorn renal stone in the left kidney. The metabolic study showed hyperuricemia and hyperuricosuria. Given the normal renal function and the disappearance of the symptoms, it was decided to start combined therapy by alkalizing the urine using *Lit-Control® pH Up*, allopurinol and dietary measures. After four months of treatment, the patient presents with uremia and uricosuria within normal values, as well as a reduction in the stone size, completely disappearing the stone that was in the upper calyx of the right kidney. The combined medical treatment for uric acid stones can dissolve the stone or reduce its size, avoiding or facilitating surgical treatment (Figure 3).

Figure 3.
Partial dissolution of left kidney staghorn stone.



Medical management of uric acid kidney stones, after a case report (Ana Morales Martínez - 1st Ed. 2020)
Urinary uric acid stones are a frequent and important pathology in our clinical practice. Conservative treatment by means of hygienic-dietary measures and correct urinary alkalinization by means of citrate and theobromine seems to be a promising combination for the treatment and resolution of these lithiasis. A case with complete resolution of a coralliform uric acid lithiasis was observed after 12 weeks of treatment with Allopurinol and *Lit-Control® pH Up* without adverse reactions and avoiding the need for invasive surgical measures. This case has been presented elsewhere as a self-standing case report after participating in the *1st Edition of Clinical Case Contest* (12).

Medical treatment of staghorn uric acid lithiasis with Lit-Control® pH Up (Baraa Nakdali Kassab - 3rd Ed. 2022)
A 65-year-old Caucasian female who was evaluated for pain in the right renal fossa of 10 days evolution, is presented. During her follow-up appointment, an abdominal/pelvic CT scan was requested where a right staghorn lithiasis of 4.5 cm x 3.2 cm was observed, occupying the upper, middle, and lower calyces, with growth towards the renal pelvis, with an average density of 450 *Hounsfield Units* (HU). An alkalizing medical treatment was started using *Lit-Control® pH Up* (potassium citrate, magnesium citrate and theobromine). After being treated for three months, the resolution of lithiasis was observed.

Table 2.
Staghorn uric acid stones.

RENAL STAGHORN STONES (N = 4)					
Author	**Patient & Stone**	**HU**	**Treatment**	**Outcome**	**Metabolic**
Laura Sánchez 2020	54 yrs M Left staghorn kidney stones	300	Lit-Control® pH Up x 2 Allopurinol Dietary measures	4 months Partial dissolution (complete dissolution of the stone in the upper calix)	High sUA High urUA
Ana Morales Martínez 2020	51 yrs F Right staghorn renal stone	436	Lit-Control® pH Up Allopurinol	12 weeks complete dissolution of the stone	High sUA
Baraa Nakdali Kassab 2022	65 yrs F Right staghorn stone 4.5 cm x 3.2 cm	450	Lit-Control® pH Up	3 months Complete dissolution	High sUA Ur pH 5.0
Isabel Mohedano 2023	52 yrs F coralliform 60 mm right stone (pelvis + middle and lower calyces)	500	Lit-Control® pH Up 1x3	11 months almost complete chemolysis	Diabetes sUA 3.1 Ur pH 5.0

Chemolytic treatment for uric acid lithiasis, even for staghorn stones, should be considered as the first treatment option. This case has been presented elsewhere as a self-standing case report after participating in the *3rd Edition of Clinical Case Contest* (13).

Chemolysis of large coralliform lithiasis with Lit-Control® pH Up (Isabel Mohedano - 4th Ed. 2023)
A case report showing the usefulness of medical treatment in coralliform lithiasis of uric acid despite its large size. A 52-year-old woman referred to our office for hematuria. An abdomino-pelvic CT scan was performed showing a 6 cm right renal lithiasis, of coralliform morphology, extending from the renal pelvis towards the middle and lower calicial groups, producing mild ectasia of the excretory system. After 11 months of urinary alkalinization using *Lit-Control® pH Up* (potassium citrate, magnesium citrate and theobromine), the patient achieved almost complete chemolysis with a pH around 6. We should consider alkalinizing pharmacotherapy as the first treatment option in patients with uric acid lithiasis (Figure 4).

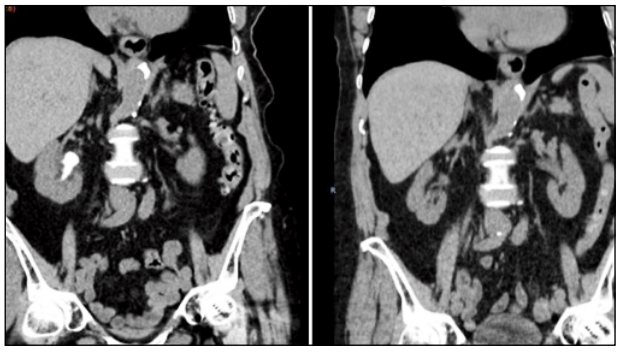
Figure 4.
Complete chemolysis of a 6 cm right renal staghorn stone.

Unilateral renal stones (Table 3)
Oral chemolysis as an effective treatment in the resolution of uric acid kidney stones
(Blanca Gómez-Jordana Mañas - 2nd Ed. 2021)
Kidney stone disease is a highly prevalent pathology that is still increasing and is composed of uric acid in 10 and 15% of cases. A clear relationship has been established between the formation of this type of stones with the presence of an acid urinary pH. Therefore, the current treatment is based on the use of urine alkalizers to prevent the crystallization of uric acid. It seems that the association of theobromine with this treatment would increase its efficacy. We reviewed a clinical case from our center that presents uric acid nephrolithiasis resolved by medical treatment (Figure 5).

Table 3.
Unilateral uric acid renal stones.

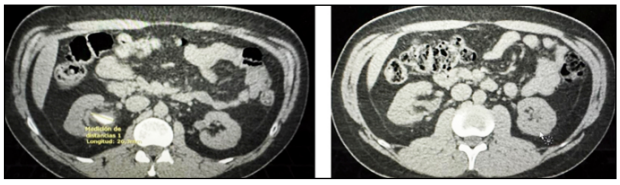
RENAL UNILATERAL STONES (N = 7					
Author	**Patient & Stone**	**HU**	**Treatment**	**Outcome**	**Metabolic**
Blanca Gómez-Jordana Mañas 2021	83 yrs F Right kidney stone 17x5 mm pelvis +lower pole stone	500	Bicarbonate poorly tolerated (high blood pressure) (3 months) Diet+lemon juice (non effective) Lit-Control® pH Up x 2	6 months complete dissolution	Ur pH 5.0
Silvia Juste Alvarez 2024	46 yrs M two stones in right pelvis (15 mm + 16 mm) + dilatation right upper-middle calyces at 6 month follow up after PCNL 27 mm stone right pelvis + two stones in lower calix (7 and 8 mm)		Lit-Control® pH Up x 2	3 months No evidence of stone	Normal sUA Ur pH 5.0
Rafael Maria Mas Lucas 2024	56 yrs F 6-7 mm stone lower left calix	NA	Lit-Control® pH up	6 months Decreased to 2 mm	Ur pH 5.0
Cristina Calzas Montalvo 2022	67 yrs F Multiple stones in right kidney (4 mm pelvis, upper, middle calix)	365	Lit-Control® pH Up x 2 300 mg of Allopurinol DJ stent	4 months Complete resolution	Ur pH 5.0 high sUA
Celia Abad Rodríguez-Hassles 2023	66 yrs F 4 mm obstructive left ureteral stone + 15 mm non-obstructive right renal pelvis stones	370	Spontaneous left stone passage + Lit-Control® pH Up 1 x 2-3 + Allopurinol 300 mg once day + DJ stent	3 months Slight decrease 6 months very significant reduction 12 months No lithiasis	Previous bariatric surgery Breast cancer mastectomy + chemotherapy + adjuvant hormone therapy sUA normal urUA 752 mg/day
Hassan Akhenaten 2024	60 yrs F two left kidney stones 15 mm in the renal pelvis and 21 mm in lower calyx		Flexible left URS Partial fragmentation Lit-Control® pH Up 2 x 2 + left DJ stent	3 months Dissolution residual stone in the lower calix	Diabetes Obesity High purine diet Mild hyperuricosuria sUA 8.5 Ur pH 5.2
Elena Mª Casas Martínez 2024	59 yrs F impacted right renal pelvis stone secondary hydronephrosis 16 x 9 mm	500	Unsuccessful Mini-PCNL (purulent urine) nephrostomy+ Lit-Control® pH Up Lit-1 x 2	2 months No evidence of stone	Low ur citrate

Figure 5.
Complete dissolution of right kidney stone 17x5 mm of the pelvis and lower pole and 3 mm stone of lower calix of left kidney.



Breaking the cycle: Successful oral treatment of recurrent uric acid stones after early post-surgical relapse (Silvia Juste Alvarez - 5th Ed. 2024)
We present a case report of an early uric acid nephrolithiasis recurrence after surgery which was successfully dissolved by oral alkalinization. We collect clinical data, laboratory studies, imaging studies (mostly CT scan) and analysis of the stone composition after surgery. Two treatments were administered sequentially during the patient's management: percutaneous nephrolithotomy was first performed, then, after an early recurrence, oral chemolysis was performed. Percutaneous nephrolithotomy was first performed due to high stone burden and obstructive uropathy. Stone composition analysis revealed uric acid as its main component. The patient suffered from early recurrence (6 months later). Oral chemolysis was decided and lithiasis was completely dissolved after alkalinization of urine with *Lit-Control® pH Up* for 3 months. The patient remains asymptomatic (Figure 6).

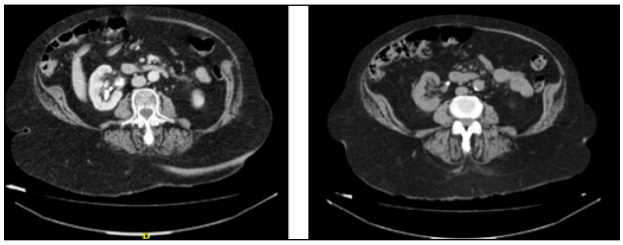
Figure 6.
Dissolution of residual stones after PCNL in the right pelvis (27 mm) and in the lower calix (7 and 8 mm).



The power of dietary supplements and urinary pH regulation in the treatment of kidney lithiasis (Rafael Maria Mas Lucas - 5th Ed. 2024)
To evaluate the effectiveness of treatment with *Lit-Control® pH Up* in reducing uric acid kidney stones and normalizing urinary pH in a patient with left renal colic. A patient with uric acid kidney stones was diagnosed through abdominal CT scan and urine analysis. After 6 months, a significant reduction in the size of the kidney stones was observed (from 6-7 mm to 2 mm), and urinary pH was normalized. The patient remained asymptomatic during this period. Treatment with *Lit-Control® pH Up* was effective in reducing kidney stone size and normalizing urinary pH, with favorable results and no new episodes of renal colic. The treatment was adjusted to maintain long-term control with a dose of 2 capsules per day.

Complete resolution of multiple nephrolithiatic pathology using conservative management with alkalizing oral chemolysis (Cristina Calzas Montalvo - 3rd Ed. 2022)
Clinical case presentation to demonstrate that uric acid lithiasis can be completely dissolved using alkalizing oral chemolysis. We describe evaluation, diagnosis, treatment, and follow-up of a 67-year-old female patient with multiple renal lithiasis who was assessed in the emergency department and later through the urology outpatient consultation. After urinary pH alkalization with *Lit-Control® pH Up* for 4 months, all the lithiasis located in the right kidney disappeared completely according to the abdominal-pelvic CT scan and the patient remains without urinary symptoms. Oral chemolysis based on urine alkalization by administration of *Lit-Control® pH Up* allows to dissolve uric acid stones if the urinary pH is kept above 7. Urinary alkalinization can be combined with allopurinol if there is hyperuricemia and/or hyperuricosuria and with urinary drainage in case of complicated renal colic or with tamsulosin to favor spontaneous expulsion (Figure 7).

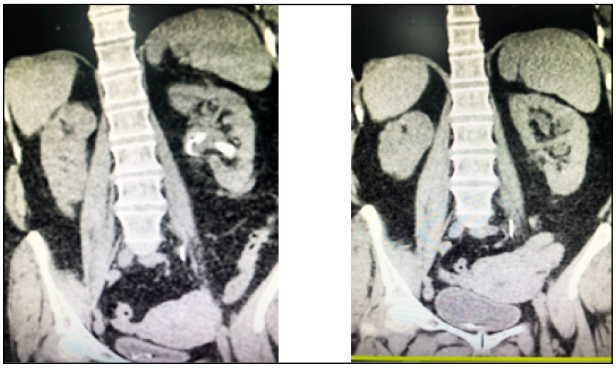
Figure 7.
Complete chemolysis of multiple stones of the right kidney.



Pharmacological chemolysis of uric acid lithiasis in a patient undergoing bariatric surgery and chemotherapy (Celia Abad Rodríguez-Hesles - 4th Ed. 2023)
A woman underwent bariatric surgery and was subsequently diagnosed with breast cancer undergoing mastectomy and chemotherapy + adjuvant hormone therapy. The patient was referred from the oncology department with left lumbar pain and an imaging test showing 4 mm of obstructive lithiasis in the left ureteral meatus together with 15 mm of non-obstructive urolithiasis in the right renal pelvis. After spontaneous expulsion of obstructive lithiasis, treatment of the right lithiasis with a composition suggestive of uric acid is proposed. The patient did not wish surgical treatment. It was decided to alkalinize the urine using *Lit-Control® pH Up* and dietary recommendations, achieving complete chemolysis. The patient currently remains asymptomatic (Figure 8).

Figure 8.
Partial dissolution of a 15 mm non-obstructive stone in the right renal pelvis.

Figure 9.
Dissolution of two stones of the left kidney (15 mm in the renal pelvis and 21 mm in lower calyx).



The role of urine alkalinization on using Lit-Control® pH Up in the treatment of uric acid kidney stones post failed endoscopic procedure. A clinical case report (Hassan Alkhatatbeh - 5th Ed. 2024)
Uric acid kidney stones are a common form of nephrolithiasis and are primarily associated with conditions such as hyperuricosuria, acidic urine pH, and obesity. The management of uric acid stones requires addressing the underlying causes, including urine alkalinization, which plays a crucial role in preventing stone formation and promoting the dissolution of existing stones. This case report explores the therapeutic benefits of urine alkalinization using *Lit-Control® pH Up* in the treatment of a patient with recurrent uric acid kidney stones with previously failed endoscopic procedure (Figure 9).

Lit-Control® pH Up prevents morbidity and mortality in Mini-PCNL treatment of large obstructive uric acid stones (Elena Mª Casas Martínez - 5th Ed. 2024)
The objective of this clinical case is to evaluate the effectiveness of *Lit-Control® pH Up* in the treatment of large uric acid stones, thus avoiding the surgical risks and complications of more invasive procedures. We present the case of a 59-year-old woman who, during an incidental imaging test, was found to have a large impacted stone in her right renal pelvis, causing secondary hydronephrosis. After an unsuccessful attempt at Mini-PCNL due to the presence of purulent urine and the visualization of a radiolucent stone on fluoroscopy, the patient was treated with *Lit-Control® pH Up* until the next surgical intervention was scheduled. During follow-up, a reduction in stone size was observed, eventually leading to its complete disappearance. Therefore, *Lit-Control® pH Up* could be considered an effective alternative therapy for the treatment of large stones, instead of more invasive interventions (Figure 10) (Table 3).

Ureteral stones (Table 4)
Clinical case presentation: pharmacological management of uric acid urolithiasis (Miguel Gómez Garberí - 1st Ed. 2020)
The prevalence of uric acid stones represents 10% of all

Figure 10.
Dissolution of a stone of the right pelvis after failed mini-PCNL.

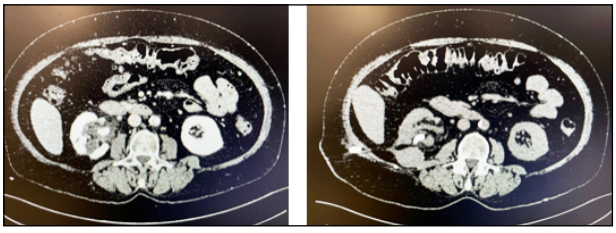


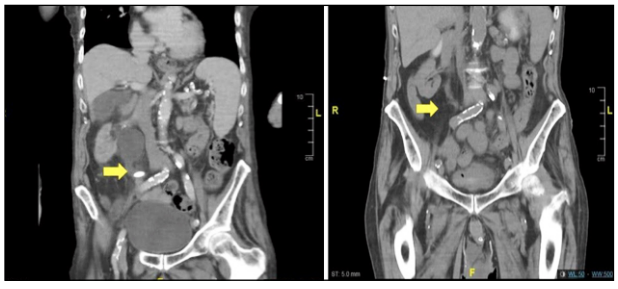
Table 4.
Ureteral uric acid stones.

URETERAL STONES (N = 5)					
Author	**Patient & Stone**	**HU**	**Treatment**	**Outcome**	**Metabolic**
Miguel Gómez Garberí 2020	67 yrs M 15 mm left ureteral stone and 22 mm left renal stone (inferior calix)		Lit-Control® pH Up Allopurinol DJ stenting	4 months complete dissolution of the ureteral stone and partial of the stone in the lower calix)	
María Negueroles-García 2021	90 yrs M 13 mm stone in an ureter loop with uretero-hydronephrosis failure of anterograde and retrograde URS		Nephrostomy oral treatment Lit-Control® pH Up 1 x 2 local chemolysis with 1/6 molar sodium bicarbonate through the nephrostomy	1 month disappearance of the lithiasis	sCr 1.64 at admission Ur pH 5.5
Daniel Carrasco Gómez 2024	60 yrs M 19 mm right lumbar ureter stones + left ureteral lithiasis of 2 mm + bilateral retrograde dilatation + lower calix microlithiasis	NA	Lit-Control® pH Up x 2 + DJ stent	3 months complete chemolysis	High sUA High urUA (980 mg/day) sCr 3.4 at entry
Leticia Ruibal Gago 2024	68 yrs M Anuria & bilateral obstruction		Canoxidin x 3 and Lit-Control® pH Up 2 x 2 Initially DJ stent (R) PCN (L) Then Bilateral PCN	Stone reduction At 4 months right RIRS	Diabetes Ur pH 5.0
Carmen Arai Valladores Ferreiro 2024	91 yrs M 15 mm pelvic renal obstructive stone of 15 mm Three obstructive ureteral stones (25 mm of length)	450-500	Lit-Control® pH Up (2 x 2 day) and sodium bicarbonate 500 mg per day Allopurinol 100 mg Low purine diet Fluid intake	At 5 months left RIRS 3 months complete dissolution of all the stones	sUA 7.4 sCr 1.7

urolithiasis and its pharmacological management has an established role in both treatment and prevention. The objective of this case presentation was to show the pharmacological management of uric acid stones. We presented a case of a 67-year-old male patient with a personal history of uric stones who attended outpatient consultation presenting kidney function deterioration and a grade III ureterohydronephrosis affecting the left kidney caused by a 15 mm obstructive stone in the proximal ureter and a 22mm non-obstructive stone in the lower calyx. It was decided to place a double-J stent and to prescribe pharmacological treatment with *Lit-Control® pH Up* and allopurinol. The complete dissolution of the intraureteral stone and a reduction of the intracalyceal stone were achieved. Pharmacological treatment can facilitate and even avoid surgical interventions in patients with uric stones.

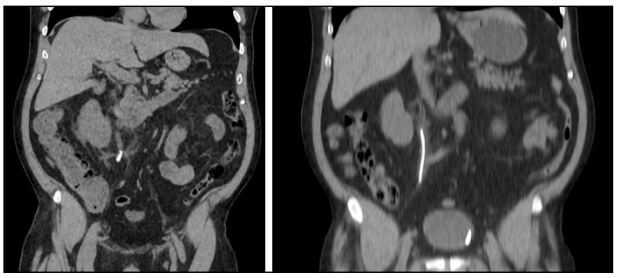
Oral and local chemolysis via nephrostomy for treatment of radiolucent stones (María Negueroles-García - 2nd Ed. 2021)
A clinical case about the use of oral and local chemolysis by nephrostomy catheter for the treatment of radiolucent stones is reported. The case of a 90-year-old multi-pathological male, who required nephrostomy due to pyelonephritis secondary to radiolucent stones in the proximal ureter, is described. After resolution of the infectious condition, surgery was attempted by anterograde and retrograde ureterorenoscopy without success because the kidney stone was found in a ureteral loop. It was decided to perform an oral treatment with *Lit-Control® pH Up* and local chemolysis with 1/6 molar sodium bicarbonate through the nephrostomy, which led to the disappearance of the lithiasis. We considered alkalizing oral chemolysis together with local nephrostomy, a useful treatment option in patients with radiolucent calculi (Figure 11).

Figure 11.
Disappearance of proximal right ureteral stone after oral treatment with Lit-Control ® pH Up and local chemolysis with 1/6 molar sodium bicarbonate through the nephrostomy.



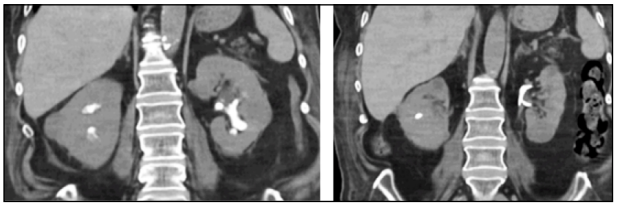
Use of Lit-Control® pH Up as alkalinizing agent for the treatment of large ureteral uric acid lithiasis (Carrasco-Gomez Daniel - 5th Ed. 2024)
To evaluate the use of medical treatment with *Lit-Control® pH Up* as a useful non-invasive alkalinizing supplement for urolithiasis. We presented the case of a 60-year-old male who came to the emergency department with typical colic caused by a 19 mm left ureteral lithiasis, producing mild ureteropelvic ectasia. After diversion of the urinary tract, CT scan control performed 3 months later just after medical expulsive treatment and *Lit-Control® pH Up* use successfully lead to resolution of that lithiasis. After 3 months of urinary alkalinization using *Lit-Control® pH Up* (potassium citrate, magnesium citrate and theobromine), the patient achieved complete chemolysis with a pH around 6. We should consider alkalinizing pharmacotherapy as the first treatment option in patients with uric acid lithiasis (Figure 12).

Figure 12.
Dissolution of right ureteral stone after DJ stenting.



Lit-Control® pH Up as a treatment for uric acid lithiasis (Leticia Ruibal Gago - 5th Ed. 2024)
This is the case of a 68-year-old man with multiple comorbidities (type 2 diabetes, epilepsy, frontotemporal dementia). He was admitted for anuria and obstructive renal failure caused by bilateral reno-ureteral stones. Initially, a right double-J stent and a left nephrostomy were placed for urinary diversion. A month later, he was readmitted due to acute renal failure and catheter obstruction, requiring replacement and the addition of a right nephrostomy. Given the urinary pH of 5 and recurrent catheter obstruction, treatment with *Canoxidin®* and *Lit-Control® pH Up* was initiated, raising the urinary pH to 6. A scheduled retrograde intrarenal surgery on the right side was performed. Following medical treatment, a reduction in left side stones was observed. Finally, retrograde intrarenal surgery on the left side was scheduled, achieving complete stone clearance. The patient remains on preventive treatment with *Lit-Control® pH Up*, with no evidence of stone recurrence (Figure 13).

Figure 13.
Reduction of size of bilateral reno-ureteral stones before RIRS.



Chemolysis in elderly and renal failure patient (Carmen Arai Valladores Ferreiro - 5th Ed. 2024)
We presented the case of 91 years old patient with personal story of frequents renal colic pain and spontaneous expulsion of lithiasis, diagnosed with multiple ureteral and renal obstructive stones compatible with uric acid composition. The patient also suffered chronic kidney failure, with creatinine clearance of 33 ml per min and potassium level of 5.3 mEq/L. We proposed chemolysis

with *Lit-Control® pH Up* (2 tablets twice a day) and sodium bicarbonate 500 mg per day, with complete dissolution of all the stones in 3 months (Table 4).

Urinary alkalinization in other pathological conditions (Table 5)
Pharmacological chemolysis of uric acid lithiasis in a patient with Crohn's disease (Rosa Maria Gras Martínez - 3rd Ed. 2022)
A male patient with Crohn's disease and an ileostomy carrier, was diagnosed with uric acid lithiasis after visiting the emergency room during an episode of left renal colic. After urinary alkalization using *Lit-Control® pH Up* and dietary recommendations, the patient achieved a complete chemolysis, maintaining the stability of his underlying condition, without showing side effects throughout the treatment. After the stone dissolution, the patient remains asymptomatic and under follow-up through outpatient visits. This case has been presented elsewhere as a self-standing case report after participating in the *3rd Edition of Clinical Case Contest* (14).

ic treatment of lithiasis using potassium citrate was planned. The patient showed partial improvement using the treatment but referred GI discomfort, so the medication was changed to *Lit-Control® pH Up* and allopurinol + colchicine, since the patient also presented hyperuricemia in control tests. Once the treatment is changed the patient showed a complete resolution of the lithiasis (Figure 14).

Figure 14.
Dissolution of left kidney stone after partial nephrectomy.

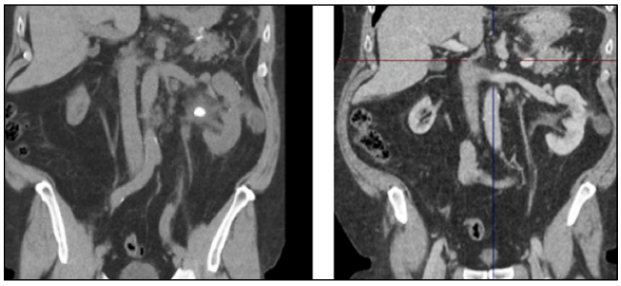


Table 5.
Urinary alkalinization in other pathological conditions.

OTHERS (N = 6)					
Author	**Patient & Stone**	**HU**	**Treatment**	**Outcome**	**Metabolic**
Rosa Maria Gras Martínez 2022	54 M Crohn disease and ileostomy 11 mm left PUJ stone	550	(Lit-Control® pH Up) x 3	12 months complete chemolitholysis	Ur pH < 5
Hector Ricardo Ayllón 2022	54 M partial nephrectomy left pelvic 16 mm stone	< 600	K citrate x 2 poorly tolerated (GI) Lit-Control® pH Up Allopurinol 300	6 months Complete resolution	Ur pH 5.5 high sUA
Sara Esturo 2023	64 yrs M Recurrent endoscopies for stone treatment resulting in critical ureteral stenosis		Allium© self expanding stent + urinary alkalinization by Lit Control® pH Up and dietary recommendations.	11-16 months slight calcification of the proximal and distal end 3 mm calcification left kidney	
Isabel Montuenga 2023	68 yrs M Single left kidney (crossed and fused renal ectopia) high volume renal lithiasis upper and middle calyces + pyelocaliceal dilatation	400-500	Lit-Control® pH Up 1 x 3 Diet & Fluid intake	significant decrease of the lithiasis load	sCr 1.46 Ur pH 5.5
Marta Casadevall 2024	70 yrs M with detrusor overactivity	NA	Lit-Control® pH Up x 2	2 months Clinical improvement Urinary frequency QoL	acidic urinary pH 6
Pedro Hernández-Peñalver 2024	77 yrs M recurrent intermediate risk non-muscle invasive bladder cancer (NMIBC) 64 yrs M multiple Ta Low Grade tumours	NA	Lit-Control® pH Up 1-2 day during the weeks of Mitomycin instillations pH monitored by the patient every day with dipsticks or *Lit-Control® pH Meter*	well tolerated urine alkalization at pH 6.0-6.5	

Lit-Control® pH Up in the medical management of uric acid lithiasis (Hector Ricardo Ayllón - 3rd Ed. 2022)
Clinical case report of a 54-year-old male, who is diagnosed with a single 16 mm kidney stone as an incidental finding in a control CT scan due to a previous left radical nephrectomy. The low Hounsfield units, urinary pH and the non-visibility of the lithiasis in simple X-ray suggested that it was a uric acid stone. After the patient's consent, chemolyt-

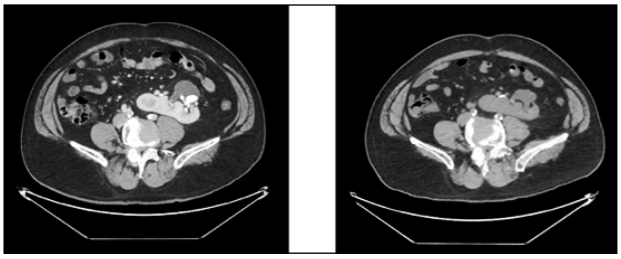
Alkalinizing treatment and urinary pH control to prevent endourological stent encrustation (Sara Esturo - 4th Ed. 2023)
The case of a man with a history of lithiasis treated with several percutaneous and endourological interventions who presented extensive critical ureteral stenosis was presented. *Allium©* self expanding stent was placed to correct the obstructive uropathy and voiding symptoms. The patency of the stent was maintained with urinary alkalin-

ization by *Lit-Control® pH Up* and dietary recommendations. The underlying pathology of the patient was stabilized with no adverse effects, good tolerance and adherence to treatment (Figure 15).

Figure 15.
Patency of a self-expanding ureteral stent was maintained with urinary alkalinization (Lit-Control® pH Up).

Chemolysis of uric acid lithiasis in a patient with crossed renal ectopia (Isabel Montuenga - 4th Ed. 2023)
A case is presented of a male patient with crossed and fused renal ectopia, who following an episode of abdominal pain, was diagnosed with high volume renal lithiasis disease associated with pyelocaliceal dilatation. Given the characteristics of the patient and the lithiasis, urinary alkalinization by using *Lit-Control® pH Up* and dietary recommendations was decided. The patient presented a clear decrease in the lithiasis load and pyelocaliceal dilatation, with no side effects. Currently, he remains with the same treatment and is being followed up in outpatient clinics (Figure 16).

Figure 16.
Almost complete dissolution of a high volume renal stone in crossed fused renal ectopia.



Urinary alkalinization for the management of overactive bladder (Marta Casadevall - 5th Ed. 2024)
Overactive bladder has a global prevalence of 10.8-35.6% and a negative impact on patient's quality of life. There is limited evidence in the literature regarding the effects that a variation in urinary pH may have on symptoms associated with overactive bladder. The aim of our study was to evaluate the clinical changes related to bladder overactivity following a treatment for urinary alkalinization. We present the case of a 70-year-old male with detrusor overactivity and acidic urinary pH (pH 6), who underwent urinary alkalinization treatment with *Lit-Control® pH Up*, monitored by an electronic device. Upon completing the treatment, clinical improvement was observed, primarily in the patient's urinary frequency, significantly enhancing his quality of life.

Urine alkalinization and measurement in patients undergoing Mitomycin instillations for intermediate risk non-muscle invasive bladder cancer (Pedro Hernández - Peñalver-5th Ed. 2024)
To explore the urine alkalinization and its measurement in patients with intermediate risk NMIBC undergoing instillations with mitomycin. Two patients were given *Lit-Control® pH Up* 1-2 times a day with a target pH ≥ 6 during the weeks prior to the instillations. Every day, they measured their urine pH with lab sticks, recording the measurements and one patient used the digital *Lit-Control® pH Meter*. *Lit-Control® pH Up* is a safe and tolerated option for improving the urine alkalinization, which aims to reduce recurrence rates in patients undergoing mitomycin instillations. The digital *pH Meter* could give more information to the patient to guide the urine alkalinization (Table 5).

Conclusions

This case series confirms the effectiveness of alkalizing therapy with citrates (*Lit-Control® pH Up*) for the dissolution of uric acid stones at any site and of any size. The time required for dissolution varied between 3 and 12 months. Side effects were mild and infrequent. High-dose citrates can cause gastro-intestinal disorders and sodium salts can aggravate urinary hypertension. The addition of theobromine may allow the dose of citrates to be reduced, increasing the efficacy and tolerability of the drug.

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Declarations

Ethical approval: *Ethics Committee (EC) was not required for a retrospective review of cases. Patient consent was obtained by the institution of each Author.*

Availability of data and material: *All inquiries can be directed to the corresponding author.*

Competing interests: *B.I. is an employee of Devicare. The remaining authors have no conflicts of interest to declare.*

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Authors' contributions: *Conceptualization, B.I. and A.T.; methodology, A.T.; software, N/A.; validation, B.I.; formal analysis, A.T.; investigation, A.T.; resources, N/A.; data curation, A.T.; writing C.A.R-H., H.A., M.B.A.B., C.A.V.F., H.R.A.B., L.B., C.C.M., N.C.G., D.C.G, M.C.R., E.M.C.M., S.E.S., L.G.M., B.G-J.M., R.M.G.M., P. H-P., S.J.A., A.L.S., R.M.M.L., I.M.S., I.M.F., B.M. de H., M.N-G., L.R.G.; writing-review and editing, A.T.; visualization, A.T.; supervision, B.I.; project administration, N/A; funding acquisition, N/A. All authors have read and agreed to the published version of the manuscript".*

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