

THE TREATMENT OF RENAL STONES IN RATIO MEDENDI BOOK BY ANTONIO DE HAEN (1716)

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ANTONIO DE HAEN

Antonius de Haen Gravenhage, December 8, 1704 - Vienna, 5 September 1776) was a Dutch physician appointed as professor and first executive board director of the University of Vienna's medical clinic.

De Haen studied medicine in Leiden and qualified as a doctor in his hometown. He was brought by his former classmate Gerard van Swieten, the personal physician of Maria Theresia, from the Netherlands in 1754 to Vienna, there he became Professor of the First Medical Clinic of the University of Vienna in the Civil Hospital. He organized the Medical University after the model of his teacher Hermann Boerhaave, away from the textbooks he was teaching medicine at the bedside of the patients. He insisted on detailed case histories and careful physical and laboratory examination before reaching a diagnosis and prescribing treatment.

He took over after the death of Van Swieten his position as personal physician of Maria Theresia. He put great emphasis in the patient observation and explored the numerous forms of fevers and was one of the pioneers of using the thermometer, the temperature fluctuations and the pulse measurement to have a valuable indication of the severity of the illness. In addition to keeping track of detailed patient case descriptions, De Haen was in favor of post mortem examination to determine the cause of death and advance clinical knowledge.

His most famous written work is *Ratio Medendi in Nosocomio Practico*, in which he mentions the 18th century Viennese hospital and numerous patient casualties. This masterpiece dedicated to Empress Maria Theresa, its not just a guide to hospital practice as the title suggests but contains numerous case histories and ranges widely over what must have been all the recognized clinical entities of the time.

The author in his book is asking himself how is possible that many men lead their lives, without the perception of the presence of the kidney stones, which often only appear post-mortem. Anton De Haen says in his script "Nature itself provides insensibility to pain, even before the resources of medical art, such as limewater of Uva Ursi"



THE USE OF UVA URSI IN MODERN MEDICINE

The Uva Ursi mentioned by the authors is commonly known as Bear Berry or with the scientific name *Arctostaphylos uva-ursi*, from the greek word *artos* (bear) and *stafulh* (grape), from the family of *Ericaceae*.

The flowers are urn-shaped, red bright, pink or white and borne in small terminal clusters. The fruits are small 5-10 mm in diameter), round, smooth, berry-like drupe looking like a miniature red apple.

The main components of ursina leaves are phenolic glucosides (5-15%), represented by 6-10% of arbutin and methylbutin, whose aglicons are made up of hydroquinone and methylhydroquinone molecules. Other constituents include ursolic acid, tannic acid, gallic acid, p-coumaric acid, syringic acid, galloylarbutin, gallo-tannins, and flavonoids, notably glycosides of quercetin, kaempferol, and myricetin.

At intestinal level, arbutin is hydrolyzed to hydroquinone and glucose; After absorption, hydroquinone is predominantly conjugated to the liver, then released into the urine as glucuronide and sulphate. Bacteria in the bladder have the ability to deconquer hydroquinone from glucuronide; The active ingredient can then perform its antimicrobial action, which has proved useful in vitro against numerous bacterial strains commonly responsible for urogenital tract infections. Other phytochemical components, such as tannins and piceoside metabolites, perform synergistic action with arbutin.

Hydroquinone has been shown to be effective in counteracting urinary infections sustained by various types of bacteria, such as *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Mycobacterium smegmatis*, *Shigella sonnei* and *Shigella flexneri*.

Hydroquinone targets bacterial cells and their quorum sensing communication systems. It has three types of activity in combinations were revealed: direct antimicrobial growth-inhibitory activity, non-specific and specific pro-quorum sensing activities, anti-quorum sensing activity.

Under the recommended use conditions Uva-ursi folium is a safe therapeutic option for treating lower urinary tract infections. There is no direct evidence, regarding human data, supporting the fact that free hydroquinone, content in the Uva-ursi leaves, causes convulsion, hepatotoxicity, nephrotoxicity, or promotion of tumors in humans

CLINICAL CASES

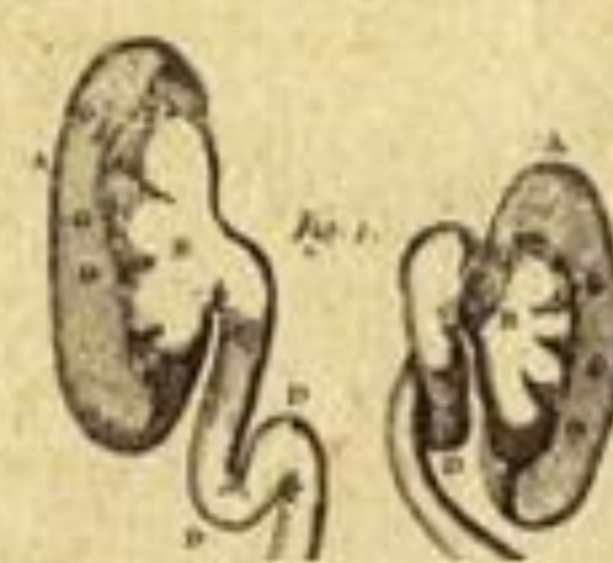
The Uva Ursi, was an adjuvant both after lithotripsy therapy and as a treatment before an invasive intervention. The author reported several exacerbation of symptomatology and reformation of calculi after the suspension of the intake of ursina grape juice and a contraction of diuresis in the immediate subsequent period.

Among clinical cases, it particularly relates to an 11-year-old child who was taken to the hospital for stranguria, which, as reported by parents, lasted for 4 years. They said that the urine came with drops of painful sorrows, fetid and with extreme effort and the child complained of urinary incontinence. Catheter exploration showed the presence of a calculus. In describing the clinical case, De Haen emphasizes the patient's unrest syndrome, typical of those with symptomatic calculi. He was slamming his feet to the ground without respite, shouted disturbin the other patients. Twice a day he gave him a dracma of ursina grapes. The benefit was so effective that the pain was almost over and had a great benefit in not get drenched and in retaini urine, there was no symptom of the presence of the calculus. After spending a month, tired of staying in the nosocomio, he asked to go back to his father's house. For the first days he had no symptoms, in the following month, for his uncontrolled diet or for failing to take the medicine at right doses, the efficacy of the drug ceased. The pains and symptoms had a recurrence. The young man was admitted for a second time at the hospital with the indication of removal the calculus. While preparing for what was needed for surgery, De Haen insisted that the operation would be deferred until the effects of the previous treatment were reinforced three times a day: half a dracma of uva ursi was somministred to him but the pain was still acute. He gave him a painkiller with barley decoction and in less than three days the pain disappeared and the subject began to urinate in a very healthy way.

After 15 days, he came back home where he had been doing his regular daily activities for two months. Abandoning the care again and not respecting the medical dictates, he fell under the previous conditions.

For the third time he was hospitalized, the benefit was lower than the previous treatment and after a few days was injected in the bladder flaxseed oil, day and night; consequently symptomatology resolved without additional injections but only with maintenance therapy with powder of ursina grapes. After one year of treatment the patient remained asymptomatic and under periodic medical check-up.

The author shows still the case of a 9-year-old boy with strangulation, oliguria and unbearable pain. A catheter exploration had found a calculation that obstructed the bladder. In two months, the illness has been resolved with the use of Uva Ursi. Oval calculation was then subsequently extracted with forceps by the surgeon. Uva Ursi also helped the patient in the post-operative course to prevent stranguria and post-operative infections.



*Immisso cathetere calculum manifeste deteximus.
Bimestri spatio incredibile quantum
uva ursina profuerit!*



CONCLUSIONS

Anton De Haen in his masterpiece shows us all the perseverance, the intuition and the knowledge that a Physician should bring in the daily clinical practice, the bedside approach to the patient and the enthusiasm of discovering new weapons against the diseases that since the dawn of medicine practice plague the society.

Thanks to his experience, he kept on using ancient remedies previously discovered by the older fathers of medicine. Even if they didn't have the correct explanation of how this methods worked and even he neather had a clear clue about Uva ursi was so relevant in the treatment the urinary diseases, his constancy rewarded him with awesome feedbacks from the scientific community of the time and from his patients, reason why we still praise him nowadays, during modern ceremonies almost three-hundreds years later.

The contribution he gave to the research inspired recent scientists to keep on looking on the use of herbs in the treatment of urinary calculi and lower urinary tract infections. These studies we reported explain how Uva Ursi leaves and his nutrient have an antioxidant potential, how they attack the target bacterial cells, their quorum sensing communication systems and the direct antimicrobial growth-inhibitory activity and the safety of his use in the clinical practice.

So after all these years we can partially answer to the question that our eminent colleague asked himself. We trust that in the same way, many of the unexplained, important questions we have in the daily medicine practice and in the scientific research, could be solved with the same strong evidences that Anton De Haen didn't have the possibilities to reach due to the sources of the time.

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