AN IDEA ON BACTERIAL LASERS AND BACTERIAL THERAPY TO TREAT KIDNEY STONES

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ABSTRACT
Kidney Stones are influenced by various factors such as deposition of calcium and uric acid, stone promoters and inhibitors. Current methods of treatment like Laser lithotripsy, Extracorporeal Shockwave therapy may be effective but have long term side effect, so enabling microorganisms (non-pathogenic) to act like laser or using them and their products to break the stones might provide a safe treatment. This treatment could be followed by continuous doses of stone inhibitor. Tamm-Horsfall(1952) protein, Diphophonates, Pyrophosphates are found to be effective stone inhibitors.

Keywords: Tamm-Horsfall protein, laser lithotripsy, GFP bacteria and beneficial soil organisms.

INTRODUCTION
Kidney stones are hard crystalline substances of calcium oxalate, calcium phosphate and uric acids; but the most common of all is calcium phosphate. The crystals are formed due to excess concentration of calcium phosphate, sodium oxalate, and urate in the body. They are found in Henles loop and few collecting ducts. Blood capillaries present in these parts, deposit excess concentration of salts. This results in the saturation of body fluid and urine which leads to crystal formation upon nucleation. It is influenced by more intakes of dairy products, low urine volume, low pH and inactivation by inhibitors. Research studies reveal that the ‘INHIBITORS’ play an important role in preventing crystal aggregation (primary promoter of kidney stones) by their repulsive electrostatic surface charge known as Zeta Potential (Doddamatikurke et al., 2007). Of all the inhibitors Osteopontin, Glycosaminoglycans, Diphophonates, Heparin, Pyrophosphate (Herbert Fleisch, 1978), Tamm-Horsfall protein was found to be an excellent inhibitor (depending on ph) (Fletcher et al., 1970; Doddamatikurke et al., 2007 and Lau et al., 2008).


With the end of introduction, the above two topics are discussed below.

Structure of Kidney Stones
On studying the structure of kidney stones, they were found to be of 2 different types-Whewellite and Wedellite (Vittorio Tazzoli et al., 1980 and Yung-Ching Chein et al., 2009). They are hydrated oxalates of calcium [CaC2O4. H2O] and [CaC2O4 (2+x) H2O]. In Whewellite, the coordination polyhedral of the pseudo equivalent atoms Ca(1) and Ca(2) are distorted square antiprisms in each of the seven of the oxygens belong to five oxalic groups and one to a water molecule. The layers are connected to one another through the second series of oxalic groups and the water molecules and form ribbons lying in the plane and running along C. In Weddellite structure, the link between these chains is made by means of (oxalate-water-oxalate) ribbons lying in parallel planes. In these ribbons the water and oxygens are bonded through hydrogen’s. Thus these structures reveal that the bonds are very strong and high energy is required to disintegrate the crystals (Wesson and Ward, 2006; De Yoreo et al., 1998 and 2006; Lauren et al., 2010). This could be achieved in the following manner-

Bacterial Therapy: A study on decay of Abies concolor shows that there are certain species of bacteria that feed or uses calcium oxalate as its substrate. Bacteria capable of utilizing calcium oxalate were obtained from decay zones of trees infected with E. trinctorium (Paul, 1979). In case of calcium oxalate crystals, these bacteria can be immobilized within biopolymer (Amjad Ali Khan et al., 2010, Dave Edell et al., 2008; Xiao- Hong Zhou, 2008 and Gatti, 2010. This biopolymer should be made specific to the environment of kidney stones, so that this biopolymer releases the bacteria only on the stones. The bacteria then adhere to the calcium oxalate crystals and consume them to finally clear the stones. However this treatment should be followed by adequate dose of antibiotics, to eliminate them from human body once their job is over. The use of these bacteria has to be made only after the pathogenicity studies.

BSOs (Beneficial soil organisms) are valuable for freeing nutrients that are in the soil but “tied up”. Most of the phosphate reserves in the soil are bonded to calcium. This Ca-P is a strong bond which...
is water insoluble. Certain strains of bacteria in soil are able to break the Ca-P bond and make the phosphate (and the Calcium) available again to the other soil life and to plants. They contain special enzymes that will break the bond between Calcium and phosphate allowing phosphorus to be available to the plant roots eg. *Azotobacter* (Shipra Garg and Bahl, 2008; Stephane Uroz et al., 2009 and Rifat Hayat et al., 2010). In case of calcium phosphate stones, these bacteria can be employed to break them. This can be done either by immobilizing the bacteria or their enzymes alone (if the bacteria is highly pathogenic), in a specific biopolymer and introducing into the body. Once the bacteria breaks the stones, the patient should be given certain amount of Vitamin C. Vitamin C binds to the phosphate released by the bacteria and prevents it from binding back to the calcium those results in stone formation (Curhan et al., 1999 and Hickey et al., 2005). The most important consideration here would be pathogenesis of the bacteria. If the bacterium is highly pathogenic then they can be genetically engineered to silence their virulence genes so that they can be safely immobilized and administered.

**Bacteria acting like LASER:** Consider a non-pathogenic bacteria that produces luminescence on its own (*shewanella woodyi*) or genetically engineered microbes that produce Green Fluoroscence Protein(GFP) Shimomura et al., 1962; Dillon and Dillon, 2004 and Pedelaq et al., 2006). Now in the cell membrane or the cell wall (preferably the cell membrane) of the glowing bacteria, mirror nanoparticles or silver nanoparticles are inserted. As the glowing light is reflected to and fro from the ends of the mirrors, the cell membrane between the mirrors would attain a metastable state (i.e the atoms of proteins, carbohydrates and lipids of cell wall). There would be multiple photon production; therefore the light obtained from it would be highly directional and monochromatic. Now this bacterium which produces high intensity beams is covered/ trapped within a biomaterial insulator (by immobilization) that is specific to calcium oxalate/uric acid crystals. This insulator would not allow the light to pass through it. It keeps them stable and steady inside.

When they are introduced (injected) into the body, the biomaterial is released and the high intensity light from bacteria acts on the stones, thus breaking them up. The bacteria here doesn’t produce high intensity light by their genes, it’s from the nanoparticles. By the time they finish acting on the stones, most of the cells would have died and the cells reproduced by them will not have this property of light. Hence they can be eliminated from the body (if required can be killed using antibiotics). Here the bacterium acts as a laser, mimicking laser lithotripsy. Here the first step of the idea is to take *Shewanella woodyi* or recombinant *E.coli* which produces GFP(or any other non-pathogenic bacteria which has GFP) (Morise et al., 1974; Prasher, et al., 1992; Stepanenko et al., 2008; Chalfie et al., 1994, Husseneder et al., 2005). Now place nano mirror particles or natural nanoparticles having unique optical properties such as ivy nano substance in the cell membrane (Lijin Xia et al., 2010).The cell membrane components act as laser media. As the light travels between the particles, it is reflected, photons are developed which come out as high directional light. This is again trapped within the biomaterial insulator (immobilization). When they are in contact with the stones, the bacteria is released. It acts on the stone with its light and hence breaks them up. After this treatment, the patient could be given doses of Tamm Horsefall protein and diphasphonates (Patel, 1964; Rutecki et al., 1971; Burg, 1976; Anwar et al., 1998) that could prevent kidney stones from re-occurring (Fig.1).

**DISCUSSION**

It has been found that the renal calculi consists of outer crystalline phase having components such as calcium, oxalates, phosphates and minute quantities of magnesium and the inner part made of organic matrix. Proteins are seen in both phases, thereby plays an important role in stone formation through protein-crystal interaction. Hence most of the crystals are covered by a layer of proteinaceous material. Here the protein stone promoters influence this reaction (Anwar et al., 1998). As a result the proteins have to be denatured using appropriate proteases. Now the crystal exposed requires strong forces to be broken. At present this has been possible through Laser Lithotripsy and Extrawave corporeal shockwave lithotripsy. Since this surgical procedure is accompanied by serious complications, we look at natural sources that have better efficiency in breaking the stones avoiding complications. Hence, here we have suggested the likelihood of treating kidney stones using bacteria. When they are suitably engineered and used, they gain the capacity of breaking the stones. Another important consideration would be preventing the re-occurrence of stones which could be accomplished by using a combination of stone inhibitors especially the ones made of proteins.

**CONCLUSION**

Earlier studies on this research were positive results. This method of using bacteria as an alternative treatment to kidney stones is only a suggestion to prevent the side effects involved in the current treatments available and also reduce its complexity. This has not been experimentally done. Further more lab research is required to standardize our idea. It’s just an idea which might help curing kidney stones when tried.
REFERENCES


**Fig-1** Bacterial Laser

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<th>Bacterial cell having GFP / other kind of bioluminscence</th>
<th>Nanomirsors are placed in the cell membrane</th>
<th>Light gets reflected within the cell membrane between the two mirrors</th>
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