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Experimental evaluation of an Ayurvedic drug on dissolution of encrustation

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ABSTRACT

Encrustation, a crust or hard coating on the surface of urinary stent & catheter, is developed due to the formation of biofilm caused by super saturation, adherence of micro bacteria and eventually deposition of mucoroteins, ions and crystals. Blockage of the stents & catheters causes reflux of urine thereby increasing renal pressure and ultimately damaging renal parenchymal tissues. El-Faqih et al has reported that encrustation occurs in 76.3% of stents left in place longer than 12 weeks. Urinary pH plays a role in the etiology of Stone formation and also for encrustation. The formation of various types of kidney stones is strongly influenced by urinary pH. An alkaline pH favors the crystallization of calcium- and phosphate-containing stones, whereas acidic urine pH promotes uric acid or cystine stones. pH/pKa of the drug reacted with different crystal forming chemicals on micro (replicated) environment Drug schedules- Dried aqueous extract of Bryophyllum pinnatum and Crataeva nurvala taken for the study. Solubility is a function of pH. Maintenance of neutral pH increases aqueous solubility. pH of Drug with different crystal forming element was between 7.5 to 7.6 .

Keywords: Encrustation, Stent, catheter, quath extract(dried water extract)

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INTRODUCTION

According to the statistics of National Kidney Foundation, kidney and urologic diseases affect at least 5% of the population and cause over 260,000 deaths per year. Among them Prostate cancer is the most common, Benign Prostatic Hyperplasia is about 10 %, Urolithiasis is about 1-15% and Bladder cancer & kidney cancer are about 50,000 &30,000 people respectively affected in each year. The people who suffer with abovementioned ailments are compelled for surgical operative measures. As a result of these surgical operations, it is mandatory on part of the Urologists to place urinary stents or catheters on routine and regular basis. When biomaterials placed in the urinary system it activates platelet growth factor leading to immunological reaction and also aggravates inflammatory markers, ultimately to development of an ulcer on urothelium. Microbacteria enters through intraurethral routes and secretes an extracellular poly saccharide matrix. That helps for the development of a biofilm. Embedded bacteria are difficult to cure as antibiotics have little role to penetrate over biofilm. Biochemical and optical analyses of stent encrustations by Robert et al revealed that these encrustations consist mainly of calcium oxalate, calcium phosphate and ammonium magnesium phosphate. According to one study the stent encrustation rate increased from 9.2% at <6 wks, through 47.5% at 6-12 wks to 76.3% at >12 weeks. Up to a 30% rate of luminal blockage has been documented with indwelling times of up to 3 months. Blockage of the stents causes reflux of urine and lead to increased renal and pelvic pressure and damages the renal parenchyma tissue. For this, the patient requires long term indwelling stents, must change the stent within 3 months of duration. Frequent changing is cost effective; require super specialized person and modern instrumentation & gives mental agony to the patient. Management of encrustation represents a continuum from therapeutic nuisance to major urologic intervention and finally it requires removal of stents and catheters and the purpose for which it was placed become defeated.

As per the literature of the Ayurvedic Texts a number of drugs have been reported for the treatment of Asmari(Urolithiasis). Varuna(Crataeva *nurvala*) and Parnabeej (Bryophyllum *pinnatum*) are among them and are being practiced by the concerned physician as well as surgeon since long[17,18, 20.] Evaluation of the drug effect was made by measuring pH/pKa of the drug reacted with different crystal forming chemicals on micro (replicated) environment.

pH is the negative logarithm of [H+] ion concentration & pKa is the acid dissociation factor. Urinary pH plays a role in the etiology of Stone formation and also for encrustation. The formation of various types of kidney stones is strongly influenced by urinary pH[1, 4]. An alkaline

pH favors the crystallization of calcium- and phosphate-containing stones, whereas acidic urine pH promotes the formation of uric acid or cystine stones [5, 10, 19] Microorganisms generate ammonia from urea, elevate the pH of urine and cause crystals of calcium and magnesium phosphates to deposit over the biomaterials .Solubility is a function of pH [2, 3] If pH is maintained to neutral then it increases aqueous solubility[1, 4.] A Drug can be efficiently solubilized by pH control should be either weak acid with low pKa or a weak base with high pKa.

MATERIALS AND METHODS

Place of the study-The study was carried out in the department of Pharmaceutics Indian Institute of Technology, Banras Hindu University, Varanasi from January 2013 to September 2013.

Collection of Chemical and Material-The analytical grade of following material used for the present study were locally purchased.

1 Calcium Phosphate

2. Calcium oxalate

3. Uric acid

4. Ethanol

5. Trial drug (Dried aq. extract of Bryophyllum pinnatum & Crataeva nurvala)

6. pH meter,

Preparation of dried aqueous extract -

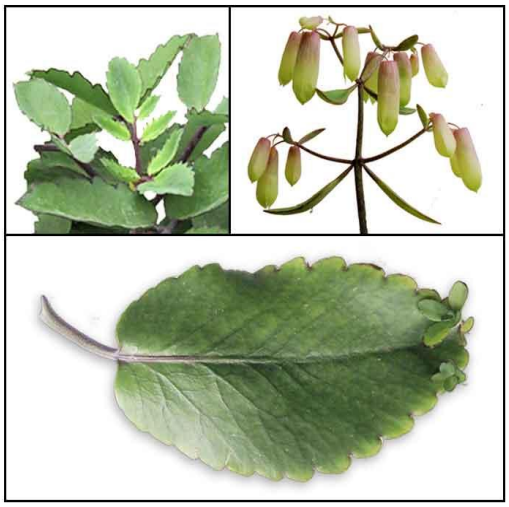


Figure 1 (Bryophyllum pinnatum)

Figure 2 (Crataeva nurvala)

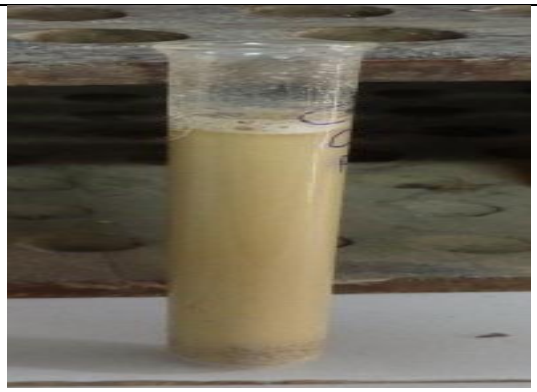
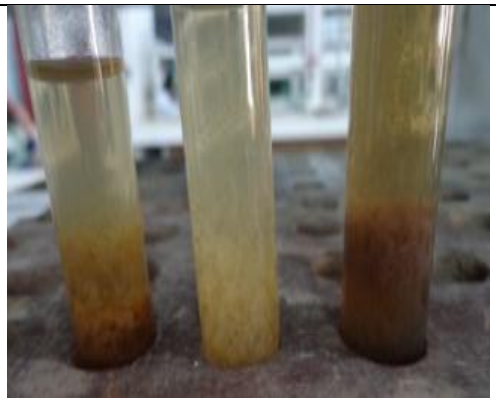
Figure 3 Crataeva nurvala

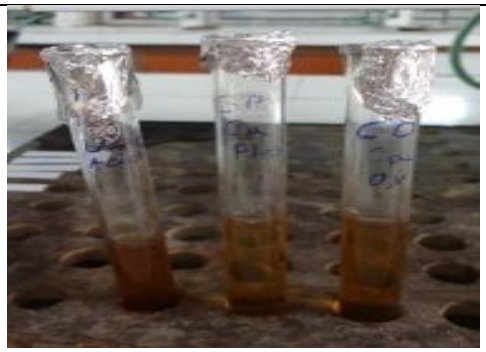
500 gm whole plant of parnabeej (Bryophyllum pinnatum) and 500gm Stem bark of Varuna (Crataeva nurvala) were procured from the local market and authenticated as per Institution norm Then the drug was cleaned and dried under shade. Kwatham (dried aqueous extract) of the above drug has been prepared separately as per the procedure mentioned in Bhaishajya Ratnavali text & Yoga Ratnakar Then the filtered substance was dried for 72-80 hrs and kept in a airtight vessel in powder form for experimental use.

Experimental Observation

Taken 10 ml of distilled water in a test tube and added equal amount chemical (stone forming element) separately (500 mg each) with same amount of drug in that test tube and kept for 24-48 hours. Then it was observed that a good amount of sedimentation was seen at the bottom of the test tube. Then it was filtered by the filter paper and then added ethanol 5 ml to each test tube and precipitation was observed. Then it was filtered, supernatant fluid discarded and precipitate material was dried and dissolved in a beaker taking 50 ml of distilled water.

Taken 500 mg of drug + 500 mg of chemical (stone forming element separately in test tube) and dissolve in 10 ml of distilled water. Kept for 24-48 hrs Shaken occasionally. (Figure 4)	 **Figure 4**

After shaking (Figure 5)	 **Figure 5**
Filtration (Figure 6)	 **Figure 6**
Added ethanol Precipitation seen(Figure 7)	 **Figure 7**

Filtration Supernatant (discarded) (Figure 8)	 **Figure 8**
Sedimentation on Filter paper &Dried in drier (Figure 9)	 **Figure 9**
Dried filter paper cut in to pices and dissolved in 50ml of beaker (Figure 10)	 **Figure 10**

For proper dis solution ultrasonicated Dissolved in 50 ml of distilled water & Ultrasonicated for 30 minute in 30 ◦ centigrade(Figure 11)	 **Figure 11**
Measured pH/pKa (Instrument shows pH is 7.70 ,but the instrument has 0.2 variation),so the pH is 7.5.(Figure 12)	 **Figure 12**
Figure 4 to 12 Experimental Evaluation	

Result of the replicated experimental study

pH/pKa of Calcium Phosphate+ Drug - 7.6

pH/pKa of Calcium Oxalate+ Drug - 7.6

pH/pKa of Uric acid+ Drug - 7.5

RESULTS AND DISCUSSION

Bryophyllum pinnatum is a good antimicrobial drug as it contains Phenolic compounds, phenolate, quinolone, Flavanoids; 5 methyl 4,5,7 trihydroxyl flavones, 4,3,5,7 tetrahydroxy 5 methyl 5 propenamine anthocyanidines and so drug acts as an antiseptic, antifungal, bactericidal. Drug also shows potent inhibition on staphylococcus aureas, Pseudomonas aeruginosa, klebsiella and candid albicans[2, 3.] Drug also inhibit cyclo-oxygenase, lipo-oxygenase pathway , there by act as an anti-inflammatory activity[8, 9] When the biomaterials are placed in-situ ,the drug may combat the bacteria to produce urease or urea amydohydralase, rendering no change in pH of the urine. The drug also reduces enzymurea, urease or urea amidohydralase [2, 3] By this no degradation of metabolic waste product to hydroxyl ion take place, hence pH of urine remain neutral. So there will be no alkalisation, no crystallization and no encrustation. As drug reduces the Ca^{2+}concentration so it can decreased encrustation. [5, 15] Drug is also containing Saponins,

Flavonoids , Glucosilinates. It also increase peak flow rate of urine as drug possess α-adrenergic receptor agonist and 5- α-reductase antagonistic activity , blocks the conversion of testosterone to dihydro-testosterone, the major hormone in prostatic cells. .The main component of crataeva nurvala is Lupeol. Lupeol proves to have good action on urolithiasis in a dose of 30mg/kg/body weight.It is a potent antiurolitholytic activity, normalizes pH and Specific gravity[5, 15.] Lupeol is proved to reduce oxalate level, reduced liver glycolate oxidase activity . As the Crataeva nurvala drug possesses Oxalate oxidase, it will help to degrade to oxalate. It catalyzes the oxygen dependant oxidation of oxalate to CO with concomittant formation of H2O2. Reduce crystallization[9, 16] It also reduce oxalate, phosphate, calcium of the plasma and urine . Drug also inhibits the release, synthesis and production of cytokines prostaglandins, histamine and polypeptide kinins and also decrease inflammation and complement activity as drug is enriched with Cadabicine& Catechin which acts as Cyclooxygenase inhibitor[8,9,10,11] -The drug also contains Fattyacids (*B.Pinnatum)* which acts as an immunomodulating effect invivo[6,7] .

Rossi Bergmann et al showed the aqueous extract of leaves cause significant inhibition of cell-mediated and humoral immune responses in mice. Saturated fatty acids present in herb plays an important role on lymphocyte proliferation, which explain its immunosuppressive effect in vivo[6, 7.] As this drug is enriched with tannin, it fasten the healing of wounds and inflamed mucous membranes. (South-eastern Nigeria use herb in treating wounds and burns) [12].

CONCLUSION

Solubility is a function of pH.. If pH is adjustable to neutral then it increases aqueous solubility. Drug is helping to bring the change of the environment of crystal to neutral pH, there by aiding dissolution followed by excretion. Drug is helping to dissolve crystal forming chemical like Calcium oxalate, Calcium phosphate & uric acid . As drug helps to maintain the urine pH to neutral thereby preventing the development of stone or encrustation on biomaterials.This drug can be applicable to prevent stone and encrustation.

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