

Experimental Study of Parameters Influencing Dissolution Kinetics of Naturally Grown and Surgically Removed Kidney Stone



Physics

KEYWORDS :

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ABSTRACT

Kidney stone formation is a biological process that involves complex crystallization phenomena. Various factors contribute to the formation of kidney stone in human body. For better understanding of mechanism of crystal growth formation, dissolution kinetics study were carried out using morphological investigation technique on naturally grown and surgically removed kidney stones.

Experimentation on these kidney stones was conducted at different temperature with various solutions and dissolution kinetics were monitored by measuring etch pit density. Dissolution parameters like activation energy, frequency factor and Gibb's free energy were calculated using Arrhenius Law.

I. Introduction

Urinary stones have afflicted mankind since ancient times. It is estimated that in India nearly 2 million people are affected with kidney stone. Also, there is a 20% probability of re-occurrence of kidney stone in such patients. There have been remarkable technological advances in the field of medical science for treatment of kidney stones. Few such examples are Lithotripsy and Endourology. However, curative techniques are frequently employed, advances in prevention or pre-mature dissolution of kidney stones has not gain pace due to our lack of understanding of the causes of stone formation.

Jungers et.al.^[1] in their work suggested that in human urine, occurrence of Calcium Oxalate Monohydrate (COM) and Calcium Oxalate Dihydrate (COD) depends also on the molar ratio of calcium and oxalate. Dorian et. al.^[2] observed evidence of aggregation in Oxalate stone formation using SEM. Recent work in this field involves studies of kidney stone dissolution using different chemicals. Dalia et. al. [3] in their work investigated ability of Hibiscus sabdariffa flower extracts to inhibit crystallization of COM crystals. Iswar Das et. al.[4] used bio-functional plant extracts in study of dissolution of tri-calcium phosphate (TCP).

Researchers all across the globe have tried various combinations of solutions and studied dissolution kinetics of kidney stones. Until the kidney stone is not surgically removed from the body and tested, exact chemical composition cannot be ascertained. There are about seven types of kidney stone identified based on the chemical composition. It is imperative for the medical practitioner to have a good judgment of the type of stone carried by the patient before administering the appropriate drug. This also makes it crucial to have a drug with universal effect and can cater to all or at least most of the type of kidney stone materials. Such a drug would remove the element of uncertainty pertaining to the type of stone material and will benefit the patient by avoiding the otherwise time lost in trial and error of combination of drugs. Also, proactive measures can then be taken easily to avoid re-occurrence of the kidney stone in future which poses a far more serious threat to the patient.

In the present work three types of kidney stone material was selected for study of dissolution kinetics under different combination of temperature and solution. Based on surface morphology and determination of etch pits width results were plotted on an Arrhenius law characteristics. Various dissolution parameters were analyzed for the given combination of input conditions and results drawn are presented here.

II. Experimentation Study

I. Experimental Setup

A glass beaker cleaned with dil. HCl solution and rinsed with distilled water was de-moisturized with the help of a hair dryer. Slices of various kidney stones were derived using a diamond based rotating round blade which runs at a uniform speed under the continuous flow of water to avoid overheating of the surface. These thick wafers were polished with fine emery paper to derive an optically reflected surface suitable for experiment and viewing under a microscope. Metallurgical research microscope with high resolution camera and labovision software tool was used to study the specimen. The software commands the camera to take a snapshot of the etched specimen and measures size and number of etch pits at the site under observation. This data is transferred to the MS Excel utility and plotted on a scatter plot diagram. Using best curve fit technique; the points were represented by a straight line interpolation equation having slope and y-intercept.

II. Methodology

Table 1 shows the parameters showing the scope of present work. Three types of kidney stone were studied with two types of solutions of varying concentrations at different temperature ranges.

Experiments were first conducted on all the three type of stones using both etchants at room temperature under different etching time of specimen. Specimen was held up in solution from 5 sec. to 35 sec. in steps of 5 sec. It was observed that maximum number of etch pits were observed at 15 sec. etching time. Accordingly, etching parameter was held constant at 15 sec. for rest of experiments.

Table 1 - Parameters of Experimental study

Kidney stone type	1) Calcium Oxalate Monophosphate COM 2) Calcium Oxalate Diphosphate COD 3) Struvite ST
Solution (varying conc. for E1)	1) Etchant E1 10ml Tri-Potassium Citrate + 10ml water 2) Etchant E2 5ml Phosphoric acid + 5 ml. water 3) Etchant E3 1ml Phosphoric acid + 9ml. water 5) Etchant E4 7ml Phosphoric acid + 3ml. water
Temperature Range	Room Temperature to 104 °C (in steps of 5 °C)

Etchant Ortho Phosphoric acid was also experimented at different concentrations viz. 1:9, 3:7 and 1:1 ratio of concentration of solution with water.

III. Observations & Discussion

III. Data analysis

Data obtained from the Labovision utility was tabulated at various temperature values. This data represents the widths of etch pits. On an average, etch pits were found in the range of 250 to 1000 nos. Of these, etch pits which were square in nature were considered for further analysis.

Data thus obtained was appropriately filtered and the average of these was taken as the reference width to plot the graph of natural logarithm of width (in microns) on y-axis and inverse of temperature (in Kelvin) on x-axis.

IV. Mathematical calculations

Graphs were plotted as shown above for the following combinations of stone material and solution. Based on the scatter plot and using best curve fitting technique straight line characteristics was drawn using the in-built functions of MS Excel utility. The resulting curve was characterized in the form of $y=mx+c$ straight line equation and represented as a combination of slope and y-intercept.

K C Poria et. al. [5] in their work on bismuth crystal demonstrated using Arrhenius law technique calculation of activation energy from the slope and frequency factor from the y-intercept of the characteristics. Also, equations for calculating entropy, enthalpy and Gibb's free energy are given in their work. On similar lines, dissolution kinetics parameters were calculated in the present study which is tabulated as shown in table no. 2 and 3.

Table 2 Dissolution kinetics parameters for Etchant 1 & 2 on different stones

Stone No.	Stone type	Etchant	Activation Ea energy	Frequency Factor A sec ⁻¹	Entropy Δ ^o S in J/Kmol	Enthalpy Δ ^o H in KJ/mol	Gibbs free energy Δ ^o G in KJ/mol
JAM. 109	ST	E1	-6893.97	0.72325	-247.98	-9479.6	67642.68
JAM. 109	ST	E2	-1479.89	5.691649	-230.83	-4065.5	67722.55
JAM. 34	COM	E1	2983.063	36.01732	-215.49	397.409	67414.98
JAM. 34	COM	E2	452.0322	12.15815	-224.52	-2133.6	67691.96
S.G. 37	COD	E1	3346.385	38.59026	-214.92	760.731	67599.89
S.G. 37	COD	E2	-5513.84	1.446288	-242.22	-8099.5	67230.94
S.G. 50	ST	E1	5296.018	83.01323	-208.55	2710.36	67568.91
S.G. 50	ST	E2	-7468.47	0.617547	-249.3	-10054	67476.71

Table 3 Dissolution Kinetic parameters for COM type stone with varying etchant concentration

Stone No.	Stone type	Etchant	Activation energy Ea	Frequency factor A	Entropy Δ ^o S	Enthalpy Δ ^o H	Gibbs free energy Δ ^o G
			KJ / mol	sec ⁻¹	J / K.mole	KJ / mol	KJ / mol
JAM. 34	COM	E3	16569.8	5100.021	-174.31	13984.1	68194.97
JAM. 34	COM	E2	452.0322	12.15815	-224.52	-2133.6	67691.96
JAM. 34	COM	E4	8063.749	149.9047	-203.63	5478.09	68808.52

As shown in Table 3 (derived from figure 9 to 11), phosphoric acid of different concentration ratio with water; 1:9; 1:1; 7:3 is taken for measuring the effectiveness of the etchant by measuring number of etch pits, width of etch pits and calculating activation energy, frequency factor, entropy, enthalpy and Gibbs free energy of COM type kidney stone (derived from figure 9 to 11). Etchant E3 has the highest activation energy and E2 has the lowest activation energy. Accordingly, increasing concentration of phosphoric acid has a bearing on improving the activation

energy only up to a certain concentration level after which the activation energy reduces. Also, frequency factor of etchant E3 is highest and of etchant E2 is lowest.

Activation Energy

- Activation energy is the minimum energy required to start a chemical reaction or as per Arrhenius law, activation energy is described as the energy required to reach the transition stage.
- From above definitions, one can conclude that the lower the activation energy, higher the reaction rate.
- From observations, highest activation energy is of the stone JAM 34 (COM) with etchant E1.
- Lowest activation energy of the stone JAM 34 (COM) is with Etchant E5.
- Negative activation energy means the rate of reaction decreases as temperature increases.
- JAM 109 (st) has negative activation energy for both the etchants.
- From literature survey (Kidney stone are more common during hot weather, but can occur any time) urine infections are most common in people with kidney stones. Infections can cause high body temperature (i.e. fever).
- From the results all the negative activation energy occurring from related drug is not good for infected people having kidney stone disease because due to infection in kidney stone the body temperature of the patient often increases and so that the rate of reaction of drug having negative activation energy will decrease. So it will take longer time to recover.
- Following data given in descending order from higher reactive to lower reactive etchant for a particular stone for negative activation energy
 - Etchant E2 for JAM 34 (com)
 - Etchant E1 for JAM 34 (com)
 - Etchant E1 for SG 37 (COD)
 - Etchant E1 for SG 50 (st)
 - Etchant E4 for JAM 34 (com)
 - Etchant E3 for JAM 34 (com)
- Activation energy is negative in following combinations of stone type & etchant obtained from different regions:
 - Saurashtra region stone no. 34 (COM) with E3.
 - South Gujarat region stone no. 37 (COD) with E2
 - South Gujarat region stone no. 50 (ST) with E2.

Frequency factor / Pre-exponential factor

- In chemical kinetics and in case of Arrhenius equation, A is the Frequency factor which shows the empirical relationship between the temperature and rate coefficient (in this case W).
- For overall results of 2 etchants and all 4 types of stones, the maximum value of frequency factor is gained for stone JAM 34 (COM) with etchant E3 while; the lowest frequency factor is obtained for stone SG 50 (ST) with etchant E2. It means that the total number of molecules per unit is higher in JAM 34 (COM) when etched with E3.

Entropy

- Change in Entropy ΔS describes the direction and measures the quantity of the magnitude of simple changes such as heat transfer between systems – always from hotter to cooler spontaneously. Therefore, the thermodynamic entropy has the dimension of energy divided by temperature and unit joule / Kelvin in SI.
- If ΔS_{sys} > 0, the system becomes more disordered through the course of reaction.
- If ΔS_{sys} < 0, the system becomes more ordered (or less disordered) through the course of reaction.
- Comparing the change in entropy for various combinations

of regions, etchants and type of stones following can be observed.

- Overall the stone SG 50 (ST) has the highest value of ΔS with etchant E2 while it has negative activation energy and lowest frequency factor.

Enthalpy

- Enthalpy is the thermodynamic potential that consists of the internal energy of the system $U+PV$ of the system.
- At constant pressure change in enthalpy is equal to energy transfer from the environment through heating.
- Total enthalpy of the system cannot be measured directly. Only change in enthalpy can be measured.
- The change in enthalpy under such conditions is the heat absorbed (or released) by the material through a chemical reaction or by external heat transfer.
- If $\Delta H > 0$, the chemical reaction is endothermic. If $\Delta H < 0$, the chemical reaction is exothermic.
- Endothermic reaction is the reaction in which the system absorbs the energy from its surroundings in the form of heat. Change in entropic energy can overcome an opposite change in enthalpic energy and make an endothermic reaction favourable.
- Exothermic reaction is a chemical or physical reaction that gives off heat. It gives out net energy to its surroundings i.e. the energy needed to initiate the reaction is less than the energy that is subsequently released.
- When the medium in which the reaction is taking place gains heat, the reaction is exothermic.
- From the calculations, both the types of enthalpy are observed.
- From result of endothermic enthalpy, following are endothermic reaction
 - JAM34 (COM) with etchant E1
 - SG37 (COD) with etchant E1
 - SG50 (ST) with etchant E1
 - JAM34 (COM) with etchant E3
 - JAM34 (COM) with etchant E4
- Rests of other are exothermic reactions.

Gibbs Free Energy

- In thermodynamics, Gibb's free energy is the thermodynamic potential that measures the "usefulness" or process-initiating work obtainable from a thermodynamic system at constant temperature and pressure (Isothermal and Isobaric).
- The Gibb's free energy is the maximum amount of non-expansion work that can be extracted from a thermodynamic closed system (on that can exchange heat and work with its surroundings but not matter); this maximum can be attained only in a completely reversible process.
- If $\Delta G < 0$; the reaction will be favoured and released energy
- If $\Delta G > 0$; then energy-in the form of work- would have to be added to the reacting system for the reaction to occur (or disfavoured reaction / non-spontaneous).
- Also, if $\Delta G < 0$, then the reaction is exergonic. If $\Delta G < 0$, then the reaction is endergonic chemical reaction
- A chemical reaction is endergonic when non-spontaneous. Thus in this type of reactions, the Gibb's free energy increases. The entropy is included in any change of the Gibb's free energy.
- From the table, all the reactions having similar value of Gibb's free energy among which Stone JAM 34 (COM) with etchant E4 reaction have highest value of ΔG while stone SG 37 (COD) with etchant E2 reaction have lowest value of ΔG . Here both the stones have same Calcium element but as they are from different regions of origin ΔG is widely apart.

IV. Conclusions

- It can thus be concluded that even if the stone types are same or they belong to the same region, their behaviour of activation energy can be different altogether.
- From the observations, it can be conclude that for combinations of stone & etchant, wherever activation energy is higher the frequency factor is also higher. Accordingly, for lower frequency factor, activation energy is also low.
- For growing the crystal the system with highly ordered behaviour is more favourable but for etching process system with less ordered behaviour is preferable. Overall etchant E2 is more likely to use than E1.

REFERENCE

- [1] Jungers P, Daudon M. "Formes cliniques de la lithiase urinaire. lithiase de l'enfant" In: Jungers P, Daudon M, Le Duc A, editors. *Lithiase urinaire*. Paris: Flammarion Médecine-Sciences; 1989. pp. 357. | [2] H.H. Dorian, P. Rez and G.W. Drach, "Evidence of Aggregation in Oxalate Stone Formation: Atomic Force and Low Voltage Scanning Electron Microscopy", *J. Urol.*, 1996, pp 1833-1837 | [3] Dalia Saleh, Samy Mahmoud, El-Sayed, "The Rate of Dissolution and Crystallization of Kidney Stone in the Presence of Hibiscus Sabdariffa Extracts", *Life Science Journal* 2013, 10(2), pp 700-710 | [4] Ishwar das, Smriti Verma "Human stones: Dissolution of calcium phosphate and cholesterol by edible plant extracts and bile acids" *Journal of scientific and Industrial research* Apr 2008, pp 291-294 | [5] K C Poria, M J Joshi, B S Shah, "Reactivity at line defects in bismuth: effect of chlorine substitution in acetic acid in the etchant", *Indian Journal of Physics* Feb. 1997, pp 593-597