CHEMOLYSIS AND EFFECT OF MANDELIC ACID (α-HYDROXYPHENYLACETIC ACID) FOR DISSOLUTION OF URINARY STONE - A STUDY IN VITRO

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A kidney stone, also known as a renal calculus (from the Latin *rēnēs*, "kidneys" and *calculus*, "pebble") is a solid concretion or crystal aggregation formed in the kidneys from dietary minerals in the urine. It was found that mandelic acid is a good inhibitor for calcium carbonate, calcium phosphate and calcium oxalate mineralization and on increasing the strength of inhibitor solution its inhibition efficiency is increased. Mandelic acid is a more efficient inhibitor for calcium carbonate salt comparing to calcium phosphate and calcium oxalate. Simultaneous dynamic model was proved to be more efficient than reservoir dynamic model. Karaunda extract is a good inhibitor for the dissolution of kidney stone. The percentage of dissolution of powder stone is more than the whole renal stone.

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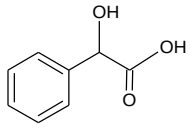
INTRODUCTION

Kidney stones are the most common painful urinary disorder. Stones can be treated by various techniques like surgical method or sound therapy method. But these treatments are highly expensive and have not been found so effective in removing the recurrence and also have side effects .It is formed when urine becomes concentrated with certain substances like calcium oxalate, phosphate, carbonate, uric acid and leaves small residues or crystals along the inner surface of the kidney. The urinary stones formation is increasing rapidly in the community and reoccurant stones become a clinical problem. The formation of urinary stones starts in our body when there is pathological disorder in our body & body start excreting excess amount of highly insoluble substances i.e. calcium phosphate , calcium carbonate and calcium oxalate. Stones can be treated by various techniques. But these treatments are highly expensive and these method give only a quick but temporary relief to the patients suffering from renal stone.

Mandelic acid is an aromatic α-hydroxy acid with the molecular formula $C_6H_5CH(OH)COOH$. It is a white crystalline solid that is soluble in water and polar organic solvents. It is a useful precursor to various drugs. Since the molecule is chiral, it exists in either of two enantiomers as well as the racemic mixture, known as paramandelic acid. Its structure is:



Mandelic acid has a long history of use in the medical community as an antibacterial, particularly in the treatment of urinary tract infections. It has also been used as an oral antibiotic, and as a component of 'chemical face peels', along with other α-hydroxy acids (AHAs).

EXPERIMENTALS

Titration Method

In titration method, we use two models i.e. simultaneous dynamic model (SDM) and reservoir dynamic model (RDM). In the SDM, the two salt forming solutions viz. sodium phosphate and calcium chloride (for calcium phosphate) and the inhibitor (mandelic acid) were taken in three separate burettes (50 ml) and were allowed to fall simultaneously into a 250 ml beaker and continuously stirred on magnetic stirrer (drop wise) with equal speed. At the end the mixture was diluted in a hot water bath for 10 minutes, cooled to room temperature and the precipitate was collected by filtering the solution through a pre-weighed Whatman's filter paper. Next, the filter paper along with the precipitate was dried in an air oven at 80°C, cooled to room temperature and weighed, the weight of the precipitate was determined.In the RDM, the whole amount of inhibitor solution (50 ml) was placed in the beaker in the beginning itself and the two salt forming solutions were allowed to run into it drop wise through burette and the reaction mixture was stirred continuously on a magnetic stirrer.

Table 1. Inhibition of calcium carbonate mineralization by mandelic acid

SALT FORMING SOLUTIONS: 0.01 M $CaCl_2$ and 0.01 M Na_2CO_3					
Inhibitor	**Conc. (M)**	**Wt. of ppt. (in grams)**		**Inhibition Efficiency (%)**	
		SDM	**RDM**	**SDM**	**RDM**
Water	-	0.0105	0.0115	-	-
Mandelic acid	0.1	0.000	0.000	100	100
Mandelic acid	0.01	0.0010	0.0032	90.4	72.7
Mandelic acid	0.001	0.0056	0.0079	41.6	31.3

Table 2. Inhibition of calcium phosphate mineralization by mandelic acid

SALT FORMING SOLUTIONS: 0.01 M $CaCl_2$ and 0.01 M Na_3PO_4					
Inhibitor	**Conc. (M)**	**Wt. of ppt. (in grams)**		**Inhibition efficiency (%)**	
		SDM	**RDM**	**SDM**	**RDM**
Water (blank)	-	0.0432	0.0444	-	-
Mandelic acid	0.1	0.000	0.006	100	98.6
Mandelic acid	0.01	0.0045	0.0136	89.5	69.3
Mandelic acid	0.001	0.0249	0.0321	43.5	27.7

Table 3. Inhibiton of calcium oxalate mineralization by mandelic acid

SALT FORMING SOLUTIONS: 0.01 M $CaCl_2$ and $Na_2C_2O_4$					
Inhibitor	**Conc. (M)**	**Wt. of ppt. (in grams)**		**Inhibition Efficiency (%)**	
		SDM	**RDM**	**SDM**	**RDM**
Water (Blank)	-	0.0482	0.0385	-	-
Mandelic Acid	0.1	0.0205	0.0215	57.4	45.1
MandelicAcid	0.01	0.0273	0.0301	43.1	21.8
MandelicAcid	0.001	0.0364	0.0322	24.4	16.3

Table 4. Dissolution of kidney stone by Karaunda extract

Obs. No.	**Sample**	**Time, h**	**Wt. of stone (in gram)**			**% of dissolution**	**Inhibitor 50 ml**
			Initial	**Final**	**Difference**		
1.	Powder stone	24	0.4254	0.3906	0.0348	8.18%	Karaunda Extract
2.	Powder stone	48	0.3906	0.2650	0.1256	32.1%	
3.	Whole stone	24	0.2007	0.1886	0.0120	6%	
4.	Whole stone	48	0.1886	0.1509	0.03773	20%	

Simultaneous blank experiment with water in place of inhibitor was also carried out for evaluating the inhibitor efficiency of inhibitor compared to water. All experiments were conducted at room temperature (30-34 °C). Percentage efficiency of inhibition (φ) of inhibitor was calculated using the formula:

$$\varphi(\%) = 100\frac{\text{(wt. of ppt. blank set) - (wt. of ppt. in expt. Set)}}{\text{wt. of ppt. in blank set}}$$

DISCUSSION

Study of Tables 1,2,3, indicates that the carbonate and phosphate of this hydroxyacid are good inhibition as compared to oxalate. The inhibition efficiency of carbonate and phosphate of this hydroxyl acid are much more than oxalate of this hydroxyl acid (mandelic acid). Sequestering of these insoluble salts by the mandelic acid might be due to complexation coupled with effective hydrogen – bonding through the -OH groups. Figure 6 indicates that the inhibitory capacity decreases with a decrease in the strength of inhibitor solution. This can be explained as the basis of mass effect. As the concentration of inhibitor decreases the equilibrium might be favouring the precipitation of insoluble salts.

A comparative study of Tables 1, 2 and 3 and Figs. 1, 2 and 3 suggests that the inhibitor is relatively less effective in the inhibition of calcium oxalate mineralization. Comparative studies of different models indicate that the simultaneous dynamic model (SDM) is the most effective one in the inhibition of mineralization. It might be due to

constant stirring, the chelating effect on Ca^{2+} ion with inhibitor and screening effect on precipitation reaction. The whole calculi were treated with 50 ml of Karaunda extract, which contains mandelic acid (50 ml Karaunda juice + 10 ml HCl). The difference in weight of whole calculus, before and after the treatment with it gave a clear indication of dissolution of some ingredients of the calculus, which remained in the solution.

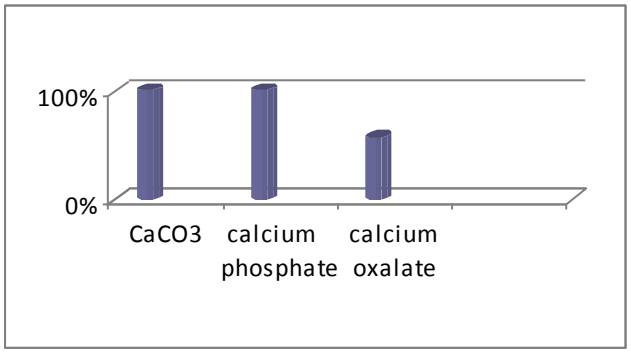


Figure 1. Simultaneous dynamic model. Inhibition efficiency of 0.1 M mandelic acid for mineralization of calcium salts

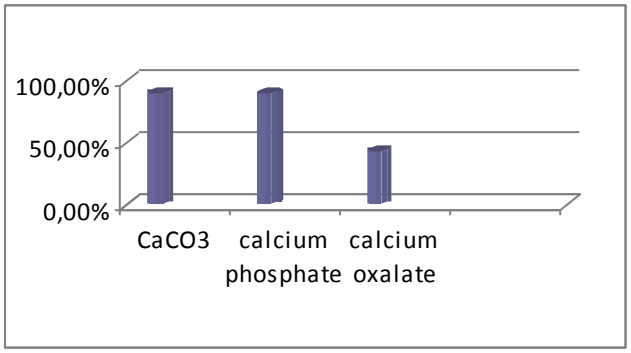


Figure 2. Simultaneous dynamic model. Inhibition efficiency of 0.01 M Mandelic acid for minerlisation of calcium salts

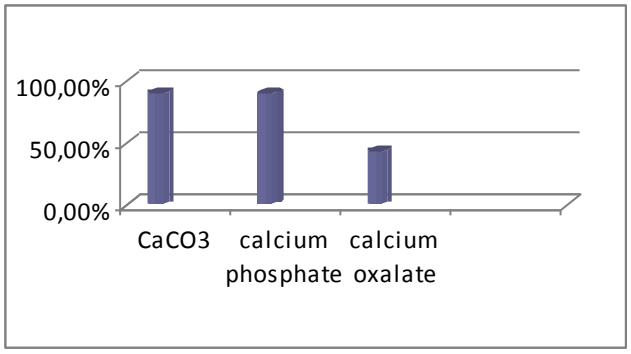


Figure 3. Simultaneous dynamic model. Inhibition efficiency of 0.001 M mandelic acid in minerlisation of calcium salts

The result of our experiment shows that the percentage solubility of the powder renal calculi is 8.1 and 31 % by the Karaunda juice per 24 hours and 48 hours respectively. Our experimental studies have indicated that by increasing the surface area of a calculus available for dissolution of reagents, the % solubility increased. The outer surface of the calculus is much more stubborn & the extract are not able to react so easily to make soluble the ingredient of the calculus. Nevertheless, the dissolution of a part of the ingredient of the whole renal calculus, definitely loosen the hardness of the calculus. This calculus then becomes very much susceptible to attach and the extract then further dissolve the calculus and the calculus crumble.

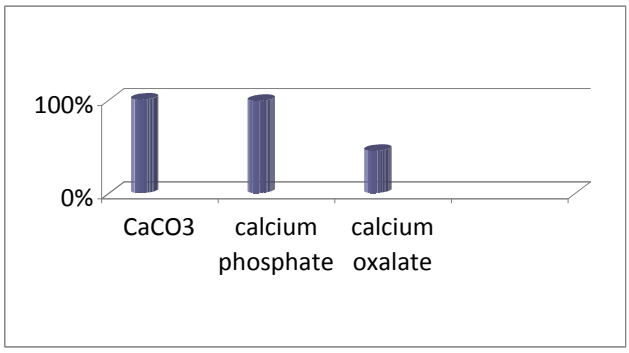


Figure 4. Reservoir dynamic model. Inhibition efficiency of 0.1 M mandelic acid in mineralization of calcium salts

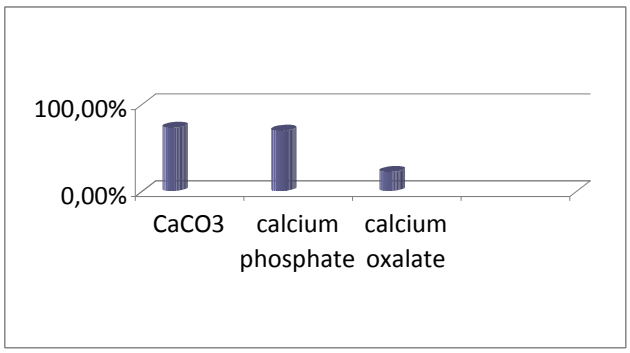


Figure 5. Reservoir dynamic model. Inhibition efficiency of 0.01 M mandelic acid mineralization of calcium salts

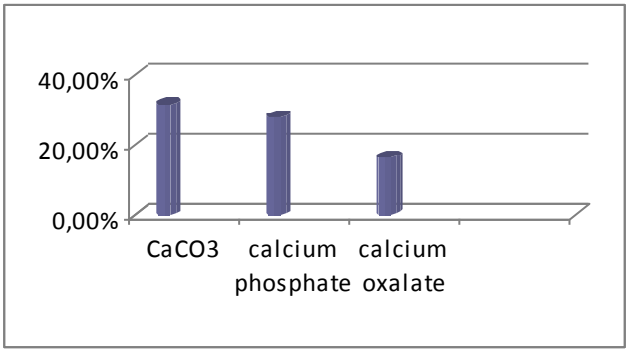


Figure 6. Reservoir dDynamic model. Inhibition efficiency of 0.001 M mandelic acid mineralization of calcium salts

CONCLUSION

The experiments that we performed clearly shows that mandelic acid is a good inhibitor for calcium carbonate, calcium phosphate and calcium oxalate mineralization.

Hence, we conclude that simultaneous dynamic model is more efficient than reservoir dynamic model.

On increasing the strength of inhibitor solution its inhibition efficiency is increased. Inhibitor (mandelic acid) is more efficient for calcium carbonate salt as compare to calcium phosphate and calcium oxalate salt. The inhibition is less effective in the inhibition of calcium oxalate mineralization by SDM with 0.1 M mandelic acid is 57.4 %. With the decrease of the strength of inhibitor the inhibition efficiency of mandelic acid decreases. Karaunda extract is a good inhibitor for the dissolution of kidney stone. The percentage of dissolution of powder stone is more than the whole renal stone.

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