IN–VITRO INHIBITION OF MINERALIZATION OF URINARY STONE FORMING MINERALS BY GLYCOLIC ACID

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The inhibition of mineralisation of urinary stone forming minerals by glycolic acid has been investigated. The inhibition efficiency of different concentration was studied. Increased intake of glycolic acid would be helpful in urinary stone prophylaxis. Glycolic acid acts as 'protecting agent'. It has been suggested that 'proteceting agents' perhaps withdraw the metal cation from solution, and thus increase the degree of 'supersaturation and it is to be expected that their addition to solution containing such ions would cause a reduction in the rate of crystal growth. Crystal growth is a very complex process since both the surface and the super saturation varies continuously throughout the period of the growth.

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Introduction

A number of people suffer from problems due to urinary stones (calculi). In India 12 % of the population is expected to have urinary stones, out of which 50 % may end up with loss of kidneys or renal damage. Also nearly 15% of the population of northern India suffers from kidney stones. Urinary stone contains both crystalloid and colloid components. The crystalloid components are mainly calcium oxalate, calcium phosphate, calcium carbonate, magnesium ammonium phosphate, uric acid and cystine. Stone formation is apparently related to the level of urinary inhibitors of calculogenesis in urine. Human urine is known to contain some protective compounds called inhibitors. These compounds sequestrate the stone and prevent the supersaturation of urine. In present work we have estimated the inhibition efficiency of glycolic acid on the mineralisation of calcium oxalate, calcium carbonate and calcium phosphate. Glycolic acid is easily available, non-toxic and does not have any side effects.

Experimental

Materials and Methods

All the chemicals used were of AR Grade. Crystalloid forming solutions viz. solution of disodium oxalate, sodium carbonate and trisodium phosphate were prepared in distilled water. Solution of 0.01 M and 0.001 M glycolic acid were also prepared in distilled water. Four experimental model namely 'Simultaneously flow static model (s.s.m), Simultaneously flow dynamic model (s.d.m), reservoir static model (r.s.m) and reservoir dynamic model (r.d.m) were designed.[1] Simultaneously blank experiments were also carried out for evaluating the inhibition efficiency of inhibitor. All the experiments were conducted at room temperature. Percentage efficiency of inhibitor was calculated.[4]

Results and Discussion

The inhibition efficiency of 0.01 M and 0.001 M glycolic acid had been investigated in different models. The results were recorded in table and Figs. 1 and 2.

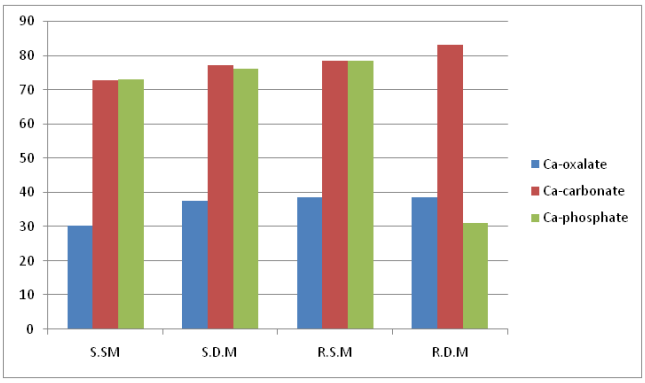

Figure 1. The inhibition efficiency of 0.01 M glycolic acid

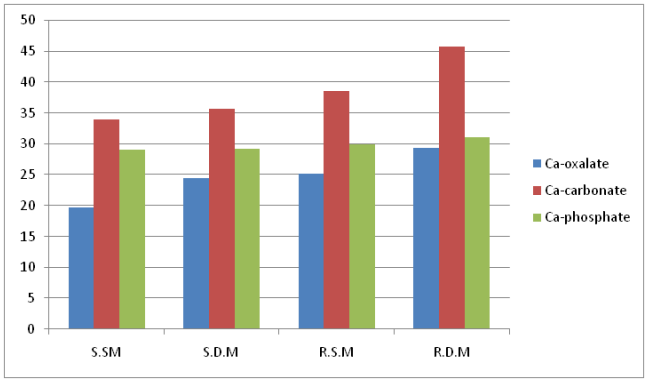

Figure 2. The inhibition efficiency of 0.001 M glycolic acid

Suspension of known weight of calcium phosphate, calcium oxalate and calcium carbonate in 100 ml deionized conductivity water were titrated conductometrically against the aqueous solution of glycolic acid. Specific conductivity for each set of titration was plotted against the volume of titrant added and the breaks in the curves were located.

Table 1. Inhibition efficiency (%) of 0.01 M and 0.001 M gylcolic acid on in vitro mineralization of urinary stone components in simultaneously flow static model (s.s.m), simultaneously flow dynamic model (s.d.m), reservoir static model (r.s.m) and reservoir dynamic model (r.d.m

Stone forming minerals	Simultaneously flow static model		Simultaneously flow dynamic model		Reservoir static model		Reservoir dynamic model	
	0.01 M	0.001 M	0.01 M	0.001 M	0.01 M	0.001 M	0.01 M	0.001 M
Calcium oxalate	30.3	19.7	37.6	25.5	38.6	25.2	38.6	29.4
Calcium carbonate	72.8	34.0	77.3	35.7	78.7	38.6	83.3	45.8
Calcium phosphate	73.1	29.1	76.3	29.2	78.5	29.9	81.8	31.1

In all the titrations specific conductivity continued to increase with the addition of titrant, however, the rate of increase of specific conductivity decreased at the break point (Figure 3a-c).

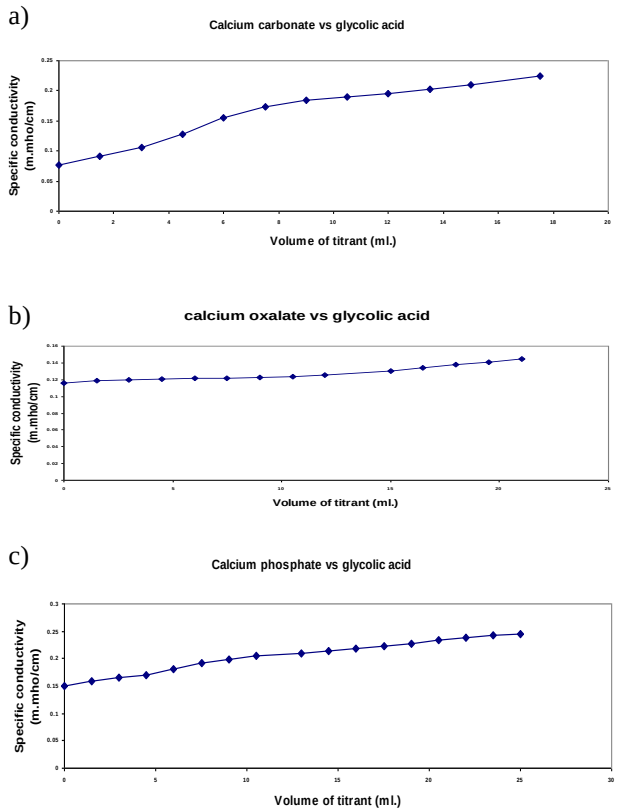

Figure 3. Titration curves of calcium salts a) calcium carbonate; b) calcium oxalate; c) calcium phosphate

Suspension of known weight of calcium phosphate, calcium oxalate and calcium carbonate in 100 ml deionized conductivity water were titrated conductometrically against the aqueous solution of glycolic acid (titation curves can be sene in the Supplementary Material). Specific conductivity for each set of titration was plotted against the volume of titrant added and the breaks in the curves were located. In all the titrations specific conductivity continued to increase with the addition of titrant, however, the rate of increase of specific conductivity decreased at the break point .

Study of the Table 1 and Figs. 1 and 2 suggests that glycolic acid is moderate to good inhibitor of calcium oxalate, calcium carbonate and calcium phosphate mineralisation. Sequestering of this insoluble calcium salts by glycolic acid might be due to effective single or mixed ligands chelation[5-6] by the hydroxyl acid present in them.

The hydroxyl acids are expected to form metal ion complexes with calcium. The presence of hydroxyl acids in urine may decrease the amount of ionised calcium available for calcium oxalate precipitate. Relatively poor inhibition of mineralisation of calcium oxalate, calcium carbonate and calcium phosphate precipitate by glycolic acid might be due to higher pka value of carbonic acid leading to replacement and precipitation of calcium salts of inhibitors rather than soluble mixed chelation.[7-8] Calcium oxalate is a stubborn constituents of urinary calculi being highly insoluble. The inhibition efficiency of oxalate is less than as compared to carbonate and phosphate.

A comparative study of different model indicates that the r.s.m model is the most effective one in the inhibition of calcium oxalate, calcium carbonate and calcium phosphate mineralisation. This might be due to mass effect.[9-10] An ab-initio presence of large concentration of inhibition (in the reservoir) coupled with continuous stirring might be effectively chelating the calcium ion and screening from precipitating anions like oxalate, carbonate and phosphate.

A comparative study also suggests that the inhibition efficiency decreases with a decrease in the strength of inhibitor solution. As the concentration of inhibitor decreases, the equilibrium might be favouring the precipitate of insoluble salts. lesser the inhibitor present less calcium ion be trapped as calcium-inhibitor complex and more calcium ions will be free for precipitate as insoluble salt. Our present study suggests that the regular intake of glycolic acid would be helpful in urinary stone prophylaxis.

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