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# Quantitative Assessment of the Effect of Additives on Nucleation, Growth and Aggregation of Crystals*

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Among the physico-chemical problems associated with biological mineralization the determination of the rates and mechanisms of nuclation, crystal growth and aggregation and the assessment of the effect of potential inhibitors/promotors thereon deserves particular attention[1]. A typical »in vivo« situation in which these processes are initiated in supersaturated, unseeded solution is crystalluria which is considered to be the initial step in renal stone formation[2]. The corresponding environment (e. g. urine) is a complex, high ionic strength solution which is generally supersaturated with respect to one or more of the mineral components of renal stone, particularly calcium oxalate hydrates and calcium phosphates. In addition urine contains a large number of ions, small and macromolecules many of which have been identified as potential inhibitors or promotors of crystallization of the urinary salts (a compilation of the relevant literature is given in ref. 1).

Although there is general agreement about the neccessity to provide clear definitions of the mode and intensity of action of »inhibitors or promotors of precipitation« no uniformity of methods has as yet been achieved. A kinetic approach developed in our laboratory[3,4] enables the investigator to distinguish between successively or simultaneously proceeding precipitation processes (nucleation, crystal growth, aggregation) and define the mode and intensity of the effect of additives on each process separately.

On the assumption of a selfpreserving distribution of sizes and shapes of particles a rate equation has been developed[3,5] which generally describes

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the kinetics of precipitation from unseeded solutions. Expressed in terms of the degree of the reaction, $\alpha$, the precipitation rate is defined as

$$(\mathrm{d}\alpha/\mathrm{d}t)\,\alpha^{-2/3} = KN^{1/3}\,S^{p} \tag{1}$$

where $N$ is the number of particles, $K$ is a constant and $p$ is the order of the reaction. $S$ is the supersaturation which can be defined in terms of solute concentrations at time $t$ and at equilibrium, $S = c_t - c_s$, or in terms of $\alpha$, $S = 1 - \alpha$. Eqn. (1) which shows the corrected precipitation rate depending on the number of particles and on the supersaturation has been found applicable to several different systems[3,6–8] in which precipitation has been initiated from unseeded solutions by heterogenous nucleation. The $\alpha$ v. s. time and log rate v. s. log supersaturation curves which are typically obtained (Figure 1) may be resolved into sections corresponding to time periods during which nucleation (increasing N, section A), crystal growth (constant $N$, section B) and growth inhibited by aggregation (decreasing $N$, section C) respectively are rate controlling. For dominant crystal growth (section B in Figure 1.) the following equations apply:

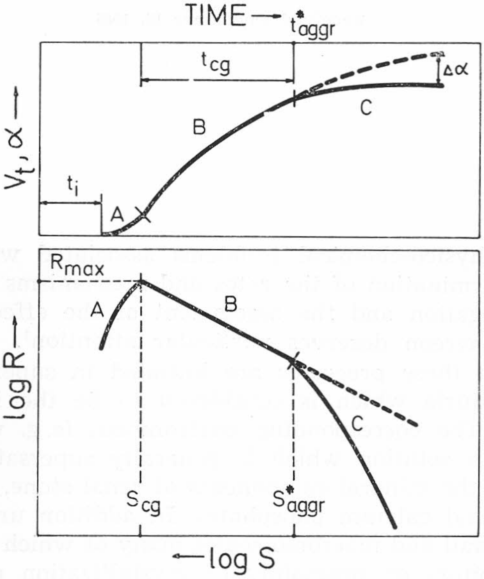

Figure 1. Schematic presentation of a kinetic precipitation experiment followed by particle size or solution analysis. (a) $V$, or $\alpha$ versus time curve and (b) rate versus supersatuartion curve (calculated after eq. (1)). Sections A, B and C correspond in time and indicate time periods in which nucleation (A), crystal growth (B) and crystal growth inhibited by aggregation (C) are rate controlling. The parameters shown are defined as follows: $t_i$ induction period, $R_{max}$ maximum precipitation rate, $S_{cg}$ corresponding supersaturation at which crystal growth assumes rate control, $t^*_{aggr}$ and $S^*_{aggr}$ critical time and supersaturation at which aggregation starts influencing crystal growth and $\Delta\alpha$ is change in $\alpha$ due to aggregation.

$$(\mathrm{d}\alpha/\mathrm{d}t)^{-2/3} = K_s\,(c_t - c_s)^{p} \tag{2a}$$

$$(\mathrm{d}\alpha/\mathrm{d}t)^{-2/3} = K_\alpha\,(1 - \alpha)^p \tag{2b}$$

where $K_s$ and $K_\alpha$ are the crystal growth rate constants.

It has been possible to define the following parameters, characterizing the kinetics of precipitation from unseeded solutions (eqns. (1), (2) and Figure 1.): the induction period ($t_i$), the maximum precipitation rate ($R_{max}$), the number of particles per $cm^3$ ($N$), the order ($p$) and rate constants ($K_\alpha$, $K_s$) of the crystal growth process, the critical time ($t_{aggr}$), the critical supersaturation ($S_{aggr}$*) and the rate constant of aggregation ($k_j$) as well as the relative changes in the surface area ($\Delta P/P$) and the degree of the reaction ($\Delta \alpha/\alpha$) due to aggregation. Details of the method have been published[3,4,9]. In ref. 9 the information which the above parameters yield on nucleation, crystal growth and aggregation is evaluated and the model is applied to the precipitation of calcium oxalate trihydrate (COT) from 0.3 molar sodium chloride solutions, with and without the presence of tryptophan or ornithine. At the given concentrations both aminoacids inhibit crystal growth and change the mode of aggregation of COT.

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## SAŽETAK

### Kvantitativna procjena efekta aditiva na nukleaciju, rast i agregaciju kristala

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Brzina spontanog taloženja iz prezasićenih otopina ovisi o broju čestica i stupnju prezasićenosti. Analizom tipičnih krivulja mogu se razlučiti stupnjevi procesa koji pokazuju nukleaciju i rast kristala, kao i rast kristala inhibiran agregacijom. Kinetika tih taložnih procesa uvjetovana je indukcijskim periodom, koncentracijom čestica, brzinom taloženja i brzinama rasta kristala, kritičnom prezasićenosti (kod koje agregacija počinje inhibirati rast kristala), brzinom agregacije te relativnom promjenom površine i stupnja reakcije kod koje dolazi do agregacije.