Urea Simulation as a Biofunctional Material

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Considering the growing interest of urea in different fields the researchers studied the simulation of growth, equilibrium, Wigner Seits and Brillouin Zone of ureea crystals. By using these methods is presented for the first time the form of this crystal related to the attachament energy and to the surface energies.

Keywords: urea crystals; growth form; equilibrium form

Urea is widely distributed in nature and its analysis is of considerable interest in clinical, pharmaceuticals and agricultural chemistry. Urea has not only clinical applications. There is a great demand of instrumentations to estimate urea in the field of food science and environmental monitoring. Urea is used as an important indicator of protein feeding efficiency for the principal component of non-protein nitrogen cow milk [1]. Urea plays a strategic role in marine nitrogen cycle, including sources of excretion by inter-vertebrates, fish, bacterial decompositions of nitrogenous material and terrestrial drainage. Urea estimations is important during environmental monitoring. Annual world production of urea is almost 100 million metric tons and majority is used as fertilizer. Urea can be the responsible for reduction of soil *p*H.

A lot of papers have been written on the relation between crystal structure and crystal morphology. Almost all of these are based on the work of Hartman and Perdok [2]. The theory of Periodic Bond Chain explains crystal morphology from the crystal structure. Intermolecular energies were taken into account and in this way prediction of the kinetic growth form was possible [3]. Hartman and Bennema introduced the proportionality of the growth rate of the F face with its attachment energy [4]. Rijpkema et al. introduced a theory based on the idea that F faces can be calculated in two dimensional Ising model where connected nets are related to critical roughening temperatures [5].

In the present paper is calculated the morphology of urea with a highly idealized structure. We present in the present paper a simulation of growth and equilibrium form of urea crystals. Wigner Seitz and Brillouin Zone analysis of urea crystals was done. The theoretical growth forms of urea are presented in this paper. Moreover, the theoretical equilibrium forms based on the specific surface energies will also be computed. In the present paper, by using these methods, is presented for the first time, Wigner Seitz and Brillouin Zone form of this crystal related to the attachment energy and to the surface energies in the crystal.

Experimental part

Material and methods

Urea crystal structure (CH_4N_2O) was studied by Caron and Donohue [6,7] and Swaminathan et al. [8]. The molecules in the structure of urea lay in a special position of the Space group P-42_1m where the molecular point symmetry is fully utilized (mm^2). The crystal structure of urea was determined by Prior, Sanger, and Gut et al. [9,10]. Urea crystal was grown from aqueous solution with a trace amount of bromide. The crystals had F forms as: {110} and {001} [11].

Parameters for the unit cell of urea , Space Group which is : P-42_1m , were traited different from different authors : Guth et al., 1980[11] considered : a = 5.572 A°, b = 5.572 A°, and c = 4.686 A° for T= 60K and a = 5.578 A°, b = 5.578 A°, and c = 4.695 A° for T= 123K, Swaminathan et al., 1984 [8] considered: a = 5.578 A, b = 5.578 A°, and c = 4.686 A° for T= 123K and Mullen and Hellner, 1978 [11] considered: a = 5.576 A°, b = 5.576 A°, and c = 4.676 A°. We used in our simulations the structure for urea crystals from Swaminathan et al., 1984 [8]

Calculations should be carried out with this structure obtained from Rietveld refinements.

The crystal structure of urea shows several chemicaly remarkable features: the molecule adopts a flat conformation in the crystal with the symmetry mm2. In contrast the isolated molecule is non planar, the NH_2 group is twisted slightly out of the molecular plane is determined by microwave spectroscopy and by initio calculations [12]. Now is accepted that C_2 molecular structure is the most stable followed by C_s conformation. C_2 structure found in the urea crystal is a saddle point separating these two stable conformers. A very interesting aspects of urea crystal is that hydrogen bonds pattern where O atom accepts four hydrogen bonds which is extremely rare. Birkedal et al reported a high precision study of charge density for urea using synchrotron data [12].

Higher order electrostatic models electrostatic moments can be calculated by the distributed multipole analysis (DMA) method . Model of potential using DMA electrostatic models and empirical repulsion-dispersion models have been applied to study the interaction of a wide range of organic molecules in the gas and crystalline phase [13]. Engkvist et al. used such models for crystallization of urea [13]. They used a variety of surface calculations using ORIENT program package to study the morphology of crystalline urea $CO(NH_2)_2$. Vapour growth of urea crystals have a well defined prismatic habit bounded by {110}, sides with {001} ends and {111} polar cap facets [13]. Engkvist et al in his work used a new nanocrystallite computational model which incorporates into ORIENT program package a variety of interaction energies and structures of surfaces and adsorbed molecules, clusters or pairs of surfaces. This method was used by Engkvist et al to predict morphology of urea crystals [13]. Based on these results we obtained in the present paper the growth and equilibrium form of

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Atom	X	Y	Z
C1	0.0	0.5	0.32821
C2	0,5	0	0,67179
O1	0.0	0.5	0.59634
O2	0.5	0	0.40366
N1	0.14468	0.64468	0.17901
N2	0.64468	0.85532	0.82099
N3	0.85532	0.35532	0.17901
N4	0.35532	0.14468	0.82099
H1	0.2557	0.7557	0.2841
H2	0.1431	0.6431	-0.0348
H3	0.75570	0.74430	0.71590
H4	0.74430	0.24430	0.28410
H5	0.24430	0.25570	0.71590
H6	0.64310	0.85690	0.03480
H7	0.85690	0.35690	0.96520
H8	0.35690	0.14310	0.03480

Table 1
POSITION OF ATOMS IN THE UNIT CELL. SPACE GROUP: P-421m; THE UNIT CELL HAS THE CONSTANTS: a = b = 5.578 A; c = 4.684 A [8]

urea crystals, to continue the results of Engkvist. In this paper from 2000 the researcher concluded that polar facets of urea crystals cannot be predicted by attachments energy model. It seems probably that large relaxation of {111} surface related to all others including {-1-1-1} inhibits the growth of these surfaces sufficiently to produce the polar caps but cannot be quantified yet [13].We used these values in our paper.

Results and discussions

Attachment and surface energies

The attachment energies including only Coulomb interactions are presented in table 2. These values are based on the charges of O,C,H and N atoms as follows :O((q_o = -2|e|), C(q_c=+4|e|), and H(q_H=+|e|); N)q_N=-3|e|).. We can see from table 2 that we can get from simulations two types of {001} as an F face. One has attachment energy higher than the other.

In table 2 we can see surface energy of urea crystals too and F faces as {200}, {101}, and {111} having two maybe three values for surface energy. In this situation is possible to have different combinations of faces and we get in for this reason more types of crystals.

Theoretical growth form of urea crystals

The theoretical growth form in this paper has been obtained by assuming that the attachment energy E_a is directly proportional to the growth rate of face (hkl). In the so-caled Wulf-Plot the length of the normal perpendicular to these faces (hkl) are then proportional to the corresponding attachment energy values.

Table 2
ATTACHMENT ENERGIES AND SURFACE ENERGY USED FOR GROWTH AND EQUILIBRIUM FORMS OF CRYSTAL

hkl	Ea(kcal/mol)	γ(kJ/m^2)
001	94.7/ 211.45	219
110	60.80	122
200	89.70	134/ 121
101	137.23	238/ 214
111	143.68	215/281/219
-1-1-1	167.54	209

(Values adapted from Engkvist et al, 2000 [14])

The growth forms presented in figure 1 A,B,C,D,E,F used the normal charges. The theoretical growth form of urea presented here shows well developed F forms as follows: {001}, {110}, {101},{200}, {-1-1-1} and {111}.

In figure 1 we can see as follows: in figure A there is a crystal having 6 F faces, 12 edges, 8 angles and a volume V= 2.8006 A^{3}and a surface S= 12.169 A^2. We can see here a well developed F forms for 001 and 110.In figure B there is an urea crystal having 10 F faces, 24 edges,16 angles and a volume of V= 6.0902 A^3, and a surface of S= 19.879 A^2. In figure B we can see very well developed F faces as follows: {001}, {200} and {111}. In figure C there is a urea crystal having 14 F faces, 36 edges, 24 angles and a volume of V= 11.692 A^3 and a surface of S= 30.393A^2. Figures A,B and C are closer to real growth form of crystals that are shown later in this paper. From simulations we obtained crystal from figure D too which has 20 F faces, 52 edges, 44 angles and a volume of V= 8.1886 A^{3}and a surface of S= 22.656 A$^{2.}$ In this crystal is missing 001 as an F face and appear faces like {101}, {200}, {111} and {-1-1-1}. In figure E we obtained from simulation a crystal with the next characteristics: 16 F faces, 32 edges, 18 angles, a volume of V= 19.936A^{3}and a surface of S= 41.710A^2. In this figure we have F faces {101}, {111} and {-1-1-1}. In figure F which seems to be closer to C is missing {001} as an F face. We obtain in figure F a urea crystal having 12 F faces, 28 edges, 18 angles , a volume V= 4.2416 A^3 and a surface of S= 16.048 A^2. We can see in figure F {101} and {110} as F faces. We can see a growth form of crystal which similar to A and is closer to B, image obtained by Boek et al. [3]. We can see a growth form of urea crystal according to Donnay -Harker presented by Boek et al. [3].

Equilibrium form of urea crystals

In figure 2, the equilibrium forms of the urea crystals are presented. These forms are obtained in idealized conditions, considering the urea crystals as purely ionic

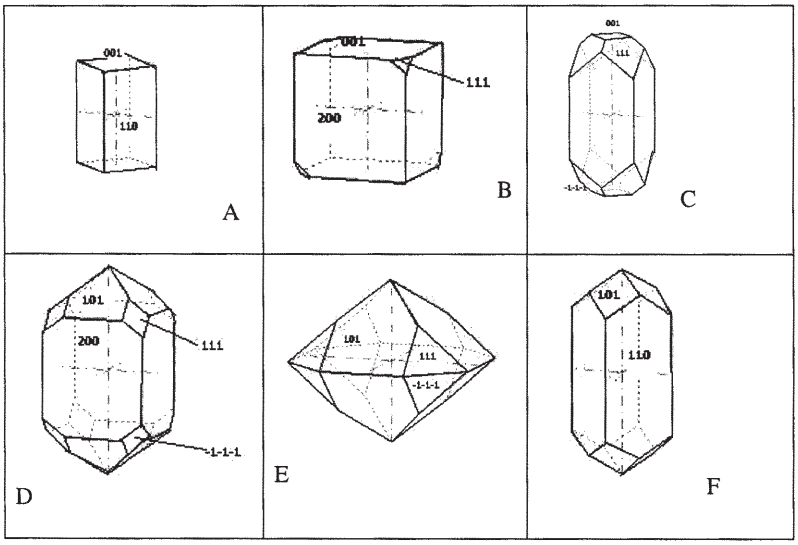

Fig. 1. Growth forms of urea crystals

compounds. The equilibrium forms shown here were constructed by using the surface energies presented in figure 3. We can see here as F forms: {001}, {110},{111},{-1-1-1}, {200} and {101}.

In figure 2 we have different types of equilibrium forms of urea crystals as follows in figure A we have an urea crystal having 22 F faces, 60 edges, 40 angles, a volume of V=28.825 A^3, a surface of S= 53.073A^2. We can see here a well developed F forms as follows {001}, {110}, {200}, {111} and {-1-1-1}. In figure B we have an urea crystal having 26 F faces, 72 edges, 48 angles, a volume of V=21.163 A^3 and a surface of S= 42.395 A^2. In figure B we can see quite similar F faces developed. In figure C from figure 2 we can see an equilibrium form for urea crystal having 26 F faces, 72 edges, 48 angles, a volume of V=20.195 A^3 and a surface of S= 40.795 A^2. In figure E we can see the equilibrium form of crystals of Boek et al.[3], which is closer as form with A,B and C, having similar F faces . In table 4 we obtain as an equilibrium form for urea crystal the form from figure D which has 16 F faces, 40 edges, 26 angles a volume of V=23.396 A^3 and a surface of S= 45.056 A^2

Wigner-Seitz and Brillouin Zone Analysis of urea crystals

In table 3 we present the results of Wigner-Seitz and Brillouin Zone Analysis of urea crystals. And in figure 3 we can observe the urea crystals obtained from these simulations. We observe from table 5 that for Wigner Seitz forms of crystals we obtained from simulation as possible F faces as follows {001}, {010}, {100}, {0-11}, {-110},{1-11},and {1-21}. We obtained from Brillouin the next F faces {001}, {010}, {100}, {011}, {110}, {-101}, {111}.

In figure 3 we obtained Wigner-Seitz and Brillouin Zone form of urea crystals. We can see here in figure A a crystal having 8 F faces, 18 edges, 12 corners, a volume of V=72.529 A^3 and surface S= 103.22A^2. In figure A we can see well developed f forms as {100}, {010} and {001}. We steel get another form of Wigner Seitz analysis of urea crystals in figure B with the next characteristics 14 F faces, 36edges, 24 corners, a volume of V=72.529 A^3 and a surface of S= 92.749 A^2. In figure B we can see the next F faces {001}, {100}, {010}, and {-110}. In figure C we have an urea crystal obtain in a Brillouin Zone Analysis having the next characteristics 6F faces, 12 edges and 8 corners with a volume of V= 6.9388 A^3 and a surface of S= 21.88

Table 3

WIGNER - SEITZ AND BRILLOUIN ZONE ANALYSIS OF UREA CRAYSTALS

hkl	E(kcal/mol)Wigner-Seitz	E(kcal/mol)Brillouin Zone
001	234.2	139.5/105.9
010	181.85	90.50
100	278.25	137.1
0-11	228.96	
-110	228.96	
1-11	228.96	
1-21	278.25	
011		139.5
110		127.1
-101		139.5
111		139.5

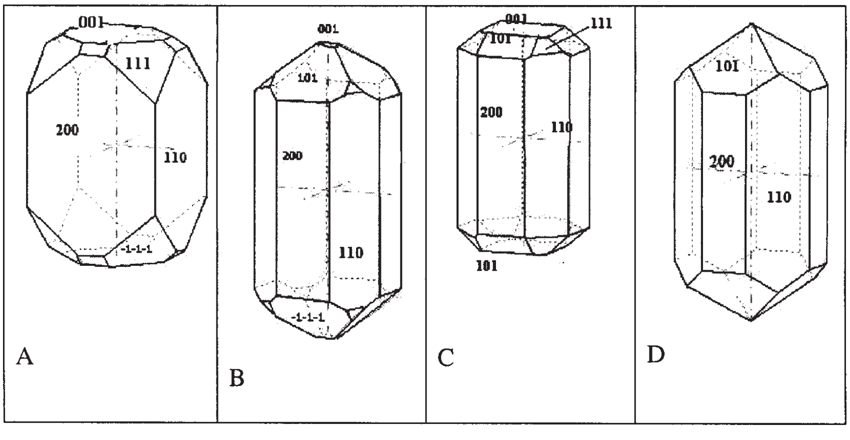

Fig. 2. Equilibrium forms of urea crystals

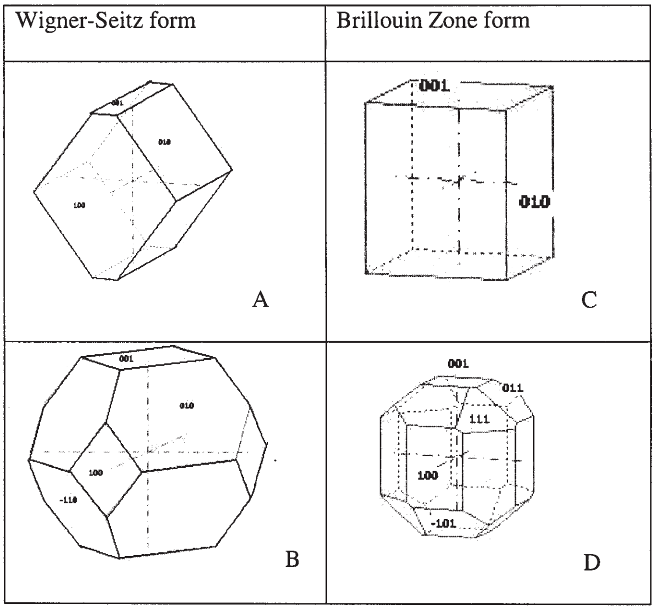

Fig. 3. Wigner-Seitz and Brillouin Zone Analysis of urea crystals

A^2. Here we can see a well developed F forms for {001} and {010}. In figure D we have another urea crystals having the next characteristics 30 F faces, 92 edges, 64 corners a volume of V=25.557 A^3 and a surface of S= 56.488 A^2. We observe from figure D well developed F faces as follows {001}, {011}, {111}, {100}, {-101}.

Theoretical growth and equilibrium forms of urea crystals ($CO(NH_2)_2$) were constructed from the calculated attachment energies which are assumed to be directly proportional to the growth rate for F faces. F forms used in growth and equilibrium form of urea crystals ($CO(NH_2)_2$) are {001}, {110},{111}, {-1-1-1}, {200} and {101}. The theoretical growth and equilibrium forms of crystaline urea were constructed from the calculated attachment energies theoretical growth forms and equilibrium forms are simulated

Attachment energy is at least for F faces directly proportional to their growth rates [4].

We observe that figure C from figure 3 looks similar to the growth form of urea crystals that we obtain from simulations and that one obtain from Boek et al. in their work. Figure B from Wigner Seitz analysis is closer of the equilibrium form of urea crystals that we obtain in figure A.

We can see in conclusion that our results from table 3 for the growth forms of crystals are in good agreement with those from Salvalaglio et al. [14] as follows: our figure A from table 3 for the growth form of urea crystal is in good agreement with case 1 from figure 1 of Salvalaglio et al., of urea crystals obtained from water. Our figure F from table 3 for growth form of urea crystals is in good agreement with case 4 from figure 1 of Salvalaglio et al. of urea crystals obtained from methanol. We can see that from table 6 with Wigner Seitz form and Brilluoin zone form of urea crystals that figure C is similar with case 1 figure 1 from Salvalaglio et al of an urea crystal obtained from water, and figure A from our figure 3 is similar with case 2 from figure 1 and case 5 figure 1from Salvalaglio et al.

The values of free energies presented in his work are related with {001}, {111} and {110} as faces obtained during growth process, the same faces that we obtained in our simulations for growth, equilibrium form, respectively for Wigner Seitz and Brilluoin Zone form of urea crystals. Piana et al. [15], reported a study of urea solvent interface at the nanometer scale . After a comparison with Piana et al results, we can conclude the following: their figure 4a – a urea crystal obtained in water as solvent is quite similar with our growth forms A and B from figure 1 and C from figure 3 which represent a Wigner Seitz form of urea crystal. We can see that figure 4b from Piana et al. that his urea crystal obtained from methanol as solvent is quite similar with our figure A from figure 3. The work of Docherty et al. explains the theoretical reasons why the morphology of urea grown from vapor possesses the peculiar polar morphology characterized by the exposition of the {001}, {111} and {110} faces. Docherty et al. [16] present in their work for the first time polar morphological prediction with the growth rate along {111} predicted to be less than {1-1-1}. A comparison of the polar morphological simulation with crystals prepared by sublimation reveals excellent agreement. We can conclude that the three forms predicted by Docherty et al. and presented in their figure 6 – case a,b and c- by using computer program HABIT with different charges for host and attaching molecules are in good agreement with our simulations of urea crystals by using the electric point charge model as follows: Case a in figure 6 from the work of Docherty et al. which represent the classical model with host and attaching molecules that have bulk atom charges [16] are in good agreement with case C from figure 1 of the growth form from our paper and case A from figure 2 with equilibrium form of crystal from our paper and and case B fromfigure 3 , the Brillouin zone form of urea crystals. Case b from figure 6 of Docherty et al which is a polar simulation with host atoms having bulk charges and attaching atoms isolated molecule charges [16] is similar with case D from our figure 3.

Conclusions

We can conclude that Wigner Seitz form represent better then Brillouin Zone, the urea crystals obtained from water, respectively from methanol and the obtained results are in good agreement with those from literature.

References

1.DHAWAN G., SUMANA G., MALHOTRA B.D., Biochem. Eng. Journal, nr. 44, 2000, p.42.

2.HARTMAN P. , PERDOK W. G., Acta Crystalogr., nr. 8, 1955, p.49; p.521; p.525.

3.BOEK E.S., FEIL D., BRIELS W.J., BENNEMA P., J.Cryst. Growth, nr. 114, 1991, p.389.

4.HARTMAN P. , BENNEMA P., J. Cryst. Growth, nr. 49, 1980, p. 145 .

5.RIJPKEMA J.J.M., KNOPS H.J.F., BENNEMA P., VAN DER ERDEN J.P. , J.Cryst.Growth , nr.61, 1983, p. 295.

6.CARON, A, DONOHUE J, Acta Cryst., nr. 17, 1964, 544-546.

7.CARON, A. , DONOHUE J., Acta Cryst. B25, 1969, 404.

8.SWAMINATHAN S., CRAVEN B.M., MCMUKKAN R.K., Acta Cryst., B40, 1984, p. 300.

9.PRYOR, A, SANGER, P. L., Acta Cryst. A26, 1970, p.543.

10. GUTH H., KLEIN G., TREUTMANN W., SCHERINGER C., Z.Kristalogr, 153, 1980,p.237.

11. MULLEN D., HELLNER E., Acta Cryst, B34, 1978, p.1624.

12.BIRKEDAL H., MADSEN D., MATHIESE R. M., KNUDSEN K., WEBER H.P., PATTINSON P., SCHWARZENBACH D., Acta Cryst., A60, 2004, p. 371.

13.ENGKVIST O., PRICE S.L., STONE A.J Phys.Chem.Chem.Phys., nr.2, 2000, p.3017.

14. SALVALAGLIO M., VETTER T., MAZZOTTI M., PARRINELLO M., Angewandte Chem. Int Ed., nr..52, 2013, p.13369.

15. PIANA S., REYHANI M., GALE J.D., Nature, nr.438, 2005, p.70.

16. DOCHERTY R., ROBERTS K.J., SAUNDERS V., BLACK S., DAVEY R.J., Faraday Discuss., n r.95, 1993, p.11

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