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Host-Guest Inclusion Complexes of α and β-Cylodextrins with α-Amino Acids†

Mahendra Nath Roy*, Deepak Ekka, Subhadeep Saha and Milan Chandra Roy

Study of molecular inclusions of a congener series of guest amino acid molecules into the host cavity of α and β-cylodextrins in aqueous solution have been focused on modern research gaining far reaching effect. With both the α and β-cyclodextrins it is found that 1:1 hosts-guest inclusion complexes are formed with all the guest molecules at both low and high pH. The variation of the thermodynamic parameters with guest size, state are used to draw inferences about contributions to the overall binding from the driving forces, *viz.*, hydrophobic effect, van der Waals force, *H*-bond, electrostatic force, structural effect and configurational theory. The formation and comparative study of inclusion complexes have been analyzed by available data supplemented with surface tension, pH, density, viscosity, and refractive index.

1. Introduction

There has been an increasing interest in the use of cyclodextrins as a tool for controlled release of active compounds due to their outstanding ability to form molecular inclusion complexes with hydrophobic guest molecules. Cyclodextrins are formed from the enzymatic degradation of starch by bacteria. They are cyclic oligosaccharides consisting of six (α-CD), seven (β-CD) and eight (γ-CD) glucopyranose units, which are bound together by α-(1-4) linkages forming a torus-shaped ring structure. Due to their unique property *i.e.*, polar hydrophilic outer shell and relatively hydrophobic inner cavity (Scheme 1), they can build up host–guest complexes by inclusion[1] of suitable hydrophobic moiety of guest molecules (*e.g.* α-amino acid). Formation of these complexes are directed to the significant applications in stabilization, carry and controlled delivery; packing effect, solubility and the reactivity of the guest molecules without any chemical modification.[2]

To the best of our knowledge and a thorough inspection of the literature reveals that no work has been carried out in present ternary solution systems. In the present study we have attempt to ascertain the nature of formation of inclusion complexes insight into the α- and β-cyclodextrins with three α-amino acids i.e., *L*-Lysine, *L*-Phenylalanine and *L*-Glutamic acid in 0.001, 0.003, 0.005 mass fractions of α- and β-cyclodextrins in aqueous media.

2. Result and Discussion

2. 1 Surface tension

Surface tension (γ) measurement can be used to obtain valuable clue about the formation of inclusion complex in cyclodextrin. It is found that γ for aqueous solutions of pure α- and β-CD do not show any remarkable change with

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†Supplementary information**:** The theory and tables (Table S1-S4) have been provided in supplementary information.

increasing concentration[3], whereas aqueous solution of *L*-Lys, *L*-Phe and *L*-Glu shows considerable variations (Fig. 1). The pH data (8.95-9.00) of aq. solution of *L*-Lys indicates the existence of $-NH_3^+$ group in both the zwitterions and end of the butylamine side chain. Due to this charged structure the ionic interaction might be occurred by NH_3^+,COO^- and end $-NH_3^+$ group of L-Lys, which reflects an increase in γ value with increasing concentration. Similar variation has been observed in surface tension of aq. solution of *L*-Glu, i.e., γ values gradually increases with increasing concentration. The fact is due to the presence of negatively charged deprotonated carboxylate ($-COO^-$) group at the side chain, as evident from pH=4.10-4.25, which is responsible for interaction in solution. But the situation is different in case of *L*-Phe, the variation of γ in aqueous solutions shows considerable decrease with increasing concentration (Fig. 1). This is because an appreciable hydrophobic nature of the benzyl ($-CH_2Ph$) group at side chain as well as hydrophilic zwitterionic group present, for which it can behave like a surfactant, which results to a decreases in the surface tension.

The surface tensions (γ) with corresponding concentration of amino acid in different mass fraction of aq. α- and β-CD have been reported for three titled α-amino acids (Fig. 1). In each case, the trends of the curves in surface tensions (γ) against concentration (molality) are similar to that of aq. amino acids, but each curve clearly shows a break point in surface tension at a certain concentration, *i.e.*, the γ values increases (*L*-Lys and *L*-Glu) or decreases (*L*-Phe) with corresponding concentration, reach a certain point (break point), and then become approximately steady, which obviously indicates the formation of inclusion complex. The formation of inclusion complexes is responsible for insertion of the hydrophobic (aliphatic or aromatic) group of chosen amino acid insight into the cavity of α- and β-CD. The possibility of the inclusion complex may have in different stoichiometries, like 1:1, 1:2, 2:1, 2:2 (Scheme 2) ratios of CD and amino acid respectively and that single break, double break, and so on in the curve of surface tension are indication of 1:1, 1:2, and so on inclusion complex by cyclodextrin.[4] In Fig. 1, each curve shows single break point, which further suggests that 1:1 inclusion complex are formed. Two intersecting straight lines have been drawn in γ, for determination of the value of γ and the corresponding concentration at the break point of the respective amino acid (Table 1). For each amino acid the change in γ is suppressed with the increasing mass fraction of aq. α- and β-CD compared to aq. amino acid, *i.e.*, the break point comes at the lower concentration of respective amino acids as well as the γ value comes closer to that of aq. CDs, which suggests that inclusion becomes feasible with increasing amount of CD in solution. If we compare between aq. α-CD and β-CD, both the values of γ and concentration at the break point are lower in case of aq. β-CD than that of aq. α-CD for *L*-Lys and *L*-Glu; but for *L*-Phe, γ is higher at the lower concentration in aq. β-CD than α-CD. This is obviously due to the fact that β-CD provides more viable feature (cavity diameter and volume) for formation of feasible inclusion complex than α-CD. The studied amino acids, thus, form soluble 1:1 complexes with both the cyclodextrins in which we visualize the nonpolar tail group of the amino acid to be inserted via the wider rim, so as to make maximum contact with the cyclodextrin cavity (Scheme 3), while the charged polar head residue remains in the wider rim of cyclodextrin or in bulk solution. This is also in correlation with the data from density and viscosity measurements, discussing underway, undoubtedly establish that β-CD is more efficient than α-CD in the formation of inclusion complexes with the above three selected α-amino acids.

2. 2 pH

The pH values of the three amino acids, *e.g.*, *L*-Lys, *L*-Phe and *L*-Glu clearly shows the existence and variation in their zwitterionic forms (Scheme 4). The pH of *L*-Lys in both aq. *α*- and *β*-CD is 9.76-10.12, suggests the existence of -NH_3^+ group in the butylamine side chain. The value of pH increases with the increasing concentration of *L*-Lys as well as with increase in concentration of *α*- and *β*-CD (table S2), indicating that after inclusion, the end -NH_3^+ group interacts with the *–OH* group of cyclodextrin by making *H*-bond (Scheme 5). The existence of side chain carboxylate –COO^- and zwitterionic group of *L*-Glu is confirmed by shifts from pH=4.10-4.25 in aq. solution to 3.16-3.40 in *α*- and *β*-CD; here the lower pH is due to release of H^+ ion from carboxylic acid (*–COOH)* group in the side chain. But the case of *L*-Phe is different; the pH range lie within 5.10-6.36 in both aq. *α*- and *β*-CD that shows simple zwitterionic structure and the rest part is hydrophobic group. Thus, *L*-Phe acts as a surfactant and is very suitable for formation of inclusion complex with the apolar cavity of CDs.

2. 3 Density

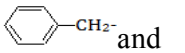
Volumetric properties, such as, apparent molar volumes, ϕ_V, and limiting apparent molar volumes ϕ_V^0, are regarded as sensitive tools for the understanding of interactions taking place in solutions. The apparent molar volume can be considered to be the sum of the geometric volume of the central solute molecule and changes in the solvent volume due to its interaction with the solute around the co-sphere. For this principle, ϕ_V have been determined from the solutions density using the suitable equation.[5] The magnitude of ϕ_V (Table S3) are found to be large and positive for all the studied systems, suggesting strong solute-solvent interactions.[6] The ϕ_V values decrease with increasing molarity (*m*) of amino acid in both the aq. *α*- and *β*-CD respectively for all the amino acids under study. ϕ_V, varies linearly with *m* and could be least-square fitted to the Masson equation[5] from where limiting molar volume ϕ_V^0 (partial molar volume at infinite dilution) have been estimated. If the variation of ϕ_V with *m* showed considerable scatter, ϕ_V^0 can be determine either graphically or taken as the average of the ϕ_V values when slope tends to zero, within the range of R^2=0.9989 to 0.9999 in linear regression coefficients and the values have been represented in table S4. The trend of variation of ϕ_V^0 of selected amino acids follows the order

Glu < Lys < Phe

The increase of ϕ_V^0 for amino acids with increasing mass fraction and the increasing positive transfer volumes suggests that the ion-ion and ion-hydrophilic group interactions are stronger than ion-hydrophobic group interactions. In the present ternary system (amino acid+ aq. cyclodextrin), the interactions of head groups (COO^- and NH_3^+) of amino acids with the cyclodextrin is localized at the *–OH* groups. Due to these interactions, the electrostriction of water caused by the charged centres of the amino acid will be reduced, which results in an increase in volume.

It is noted (Fig. 2) that ϕ_V^0 of *L*-Glu is less than that of *L*-Lys owing to greater electrostriction. This is because the additional methylene groups (with increasing chain length) provide an increasing structure enforcing tendency in *L*-Lys, and as a result, the water in the overlapping co-spheres is more structured than in the bulk. When this water relaxes to the bulk, there is a decrease in volume. But, in amino acids, the interactions increase with the addition of -CH_2 groups, and consequently there is a net increase in volume.

The results on chosen amino acids can be rationalizing on the basis that the partial molar volume is observed to increase with the increasing molar mass and size of the amino acid (Table S4). The ϕ_V^0 for glycine, *L*-alanine, *L*-valine has been studied earlier.[6] When one *H* of *L*-Ala is replaced by a $-(CH_2)_4NH_2$ (*L*-Lys), $-CH_2C_6H_5$ (*L*-Phe), $-(CH_2)_2COOH$ (*L*-Glu) groups, there is a huge change in ϕ_V^0, this should increase by virtue of its increased chain length as well as size. *L*-Glu has a hydrophobic $-(CH_2)_2$ and hydrophilic acid (*–COOH*) group, because of which the ϕ_V^0 is less compatible to *L*-Lys (containing a hydrophobic $-(CH_2)_4$ and hydrophilic ($-NH_2$) group), though they have almost same molar mass. When a $-CH_2$ group (*L*-Ala) is replaced by a hydrophobic $-(CH_2)_2$ group (*L*-Glu), ϕ_V^0 increases because of the structure-enhancing behavior of the alkyl group. If $-(CH_2)_2$ group of (*L*-Glu) is replaced by another hydrophobic $-(CH_2)_2$ group (*L*-Lys), the increase in the partial molar volume should be more, relative to *L*-Glu owning to greater hydrophobicity of the side chain, as it observed. On the other hand, *L*-Phe has the maximum value of ϕ_V^0 in the series of studied amino acids, which can be attributed to its great effect of both the zwitterions and benzyl ($-CH_2C_6H_5$) group as well as largest size and mass.

The entire group present in the studied amino acids (*L*-Lys, *L*-Phe, and *L*-Glu) greatly effect in the inclusion complexes occurring in the solution systems. Variations of ϕ_V^0 and viscosity *B*-coefficient with the number of carbon atoms (n_c) in the alkyl chain for basic, neutral, acidic amino acids in presence of α- and β-CD have been estimated (Table 2). It is observed that, for chosen amino acids, while the slopes are the volume contributions by the CH_2 group found within the range of 7.34-20.11 $\times 10^{-6}$ m^3 mol^{-1} to ϕ_V^0, which is of the order reported for amino acids in water (16×10^{-6} m^3 mol^{-1})[7] and the intercept, the volume contribution by polar head groups stay in range of 23.11-34.94$\times10^{-6}$ m^3 mol^{-1}. For *L*-Lys the contribution of (NH_3^+, COO^-) to ϕ_V^0 is larger than that of the $-CH_2-$ group and decreases with the increase in the mass fraction (w_n) for both the α- and β-CD, that designates the interactions between the *–OH* group (primary of secondary) of CD and polar head groups (NH_3^+, COO^-) of amino acids are strong; but decreases with increasing mass fraction of α- and β-CD. The contribution of $-CH_2$ group increases, which suggests that $-CH_2$ group exerts the *+I* effect. For a particular mass fraction (say w_n=0.001), contribution of (NH_3^+, COO^-) groups for *L*-Lys is less significant than *L*-Phe, which in turn lesser than *L*-Glu; which advocates that the (NH_3^+, COO^-) group contribution is effective for *L*-Glu. However, the $-CH_2$ group contribution has been found to the opposite trend, i.e., contribution of $-CH_2$ group is greater for *L*-Lys than *L*-Phe, which in turn greater than *L*-Glu; which suggests that the $-CH_2$ group exerts the *+I* effect, as a result of increasing number of $-CH_2$ groups interactions are more fascinated. If we consider the other group for *L*-Lys, the contribution of $-(CH_2)_4NH_2$ group increases with increasing the mass fraction of both the α- and β-CD, but for $-NH_2$ group it decreases, that means the effect of hydrophilic end $-NH_2$ group is very poor, whereas $-(CH_2)_4NH_2$ is more effective due to the more number of $-CH_2$ groups and also greater the *+I* effect. For *L*-Phe, contribution of both  and  to ϕ_V^0 are found to be greater and increases with in mass fraction of CD; that proposes both the groups strongly effect with the hydrophobic solvation as well as side chain phenyl group effect. For *L*-Glu both the $-(CH_2)COOH$ and end *–COOH* group contribution are increases with rising amount of mass of CD in solution, that implies that both group are contributed as similar fashion. Between these two the contribution of *–COOH*

are higher than $–CH_2$, entailed that hydrophilic end $–COOH$ are stronger.

A decrease in hydration number (n_H) and increase in solvation number (S_n) on addition of α-and β-CD (Table 3) is due to the decrease in the electrostriction of water. *L*-Lys with a larger charge separation, greater hydrophobicity and $+I$ effect, than *L*-Glu has a larger value of solvation number, which is consistent with the results of Ogawa et. al.[8] Due to large electrostriction, greater effect of $-CH_2C_6H_5$ group in the case of *L*-Phe, solvation numbers are found to be higher than in the other amino acids studied. The table 3, also state that *L*-Lys is more solvated by CD than *L*-Glu. If we consider individual cyclodextrin, initially in aqueous mixture all or maximum of $–OH$ (primary or secondary) groups interact with the water molecules present in the bulk solution. After addition of chosen amino acids (separately), they fascinated the $–OH$ by replacing the water molecules with the proper phase of interaction, as zwitterionic groups, end $–NH_3^+$ group of butylamine of *L*-Lys, side chain $–COO^-$ group of *L*-Glu, and benzyl group ($-CH_2C_6H_5$) of *L*-Phe; as a result there is a net increase in solvation number. Lower the hydration numbers as well as higher the solvation numbers in β-CD than α-CD for studied amino acids further suggests that β-CD are more fascinated for solvation than α-CD.

2. 4 Viscosity

The viscosity of aq. CD increases with an increase in employed mass fraction w=0.001, 0.003 and 0.005 (table S1), attributed to the structure-making influence between CD and water by breaking the *H*-bonded structure of water in its vicinity. For the ternary system (amino acid+aq. CD), at a given concentration of CD, the viscosity of the solution increases with the increasing molarity of amino acids (table S2). The viscosity *B*-coefficient is known to depend[9] on the size and shape of the solute molecules also indicates the solute-solvent interactions. The *B*-coefficients of all the studied amino acids were positive (Fig. 3) and increases with the increasing concentration of CD, which may be considered to arise due to increasing amino acid-cyclodextrin interaction as well as increase in solvation.

The group contributions of the amino acids to viscosity *B*-coefficient have been derived using the same scheme as Ekka et. al.[6] From table 2 it is seen that $B(NH_3^+, COO^-)$ for *L*-Lys and *L*-Glu decreases and $B(-CH_2)$ values decreases with increasing mass fraction (w_n) of both CD, suggesting the effect of (NH_3^+, COO^-) groups are diminished and that of $–CH_2$ groups are enhanced in the structure for solute-solvent interactions in solutions. The side chain contribution shows the positive and greater for *L*-Phe than *L*-Lys, which in turn greater than *L*-Glu. The fact is due to the structure making propensity and these findings are found to be the same trend as discussed in group contribution to volume.

2. 5 Refractive index

The refractive index and molar refraction is also a valuable tool for investigating the molecular interaction in solution. More refractive index implies the velocity of light becomes less through the medium, in other words, more molar refraction (R_M) as well as limiting molar refraction (R_M^0) (table S3 and S4) indicates that the medium is denser or more compact.[10] Therefore, from Fig. 4 it is evident that the inclusion complex of *L*-Phe with both the α- and β-CD is more closely packed than that of *L*-Lys and *L*-Glu. This may be explained as because of grater hydrophobic interaction between the $–CH_2Ph$ group of *L*-Phe and the hydrophobic cavity of α- and β-CD, than that of $–(CH_2)_n–$ group present in *L*-Lys and *L*-Glu. This reflects that the inclusion complexes formed by *L*-Phe are denser and stronger, which is in good agreement with the data found from surface tension, density and viscosity.

2. 6 Structural influence of Cyclodextrins

Complex formation is a dimensional fit between host cavity of CD and amino acid molecule. The most notable feature of cyclodextrin molecule (lipophilic cavity diameter of α- and β-CD is 4.7-5.3Å and 6.0-6.5Å respectively) provides a micro environment into which appropriately sized non-polar moiety enters and form strong inclusion complexes[11] (Scheme 5). But, no covalent bonds are broken or formed during formation of the inclusion complex.[12] The main driving force in aqueous solution is that the slightly apolar cyclodextrin cavity is occupied by water molecules[3] which are energetically unfavoured (polar-apolar interaction), therefore can be readily substituted by more hydrophobic side chain group of α-amino acid molecules which is less polar than water, to attain an apolar–apolar association and decrease of cyclodextrin ring strain resulting in a more stable lower energy state.[13] One or two cyclodextrin molecules can entrap one or more amino acid molecules; therefore, the plausible host:guest ratio of the inclusion is 1:1, 1:2, 2:1, and 2:2, or even more complicated association complex, and higher order equilibria can exist simultaneously (Scheme 2). However, the simplest and most frequent case of host:guest ratio is 1:1 by the spirit of molecular encapsulation by α- and β-CD has been observed from surface tension and related studies discussed above. Also it is difficult for a second amino acid molecule to trap by the cavity of the cyclodextrin after inclusion of a molecule. This is because, the cavity size (Scheme 1) and volume allow a single molecule to accommodate through the wider or secondary rim and both the narrow and wider rims are blocked (Scheme 3 and 5). The inclusion result states that the binding strength of *L*-Phe-CD complex is well fit together on specific local interactions between surface atoms and form strong inclusion than *L*-Lys-CD and *L*-Glu-CD.

Based on these dimensions of the α- and β-cyclodextrins the selected amino acids can typically complex with aliphatic, aromatics side chains. Hence, the positive interactions occurred to form the inclusion complex by

- The displacement of polar water molecules from the apolar cavity of cyclodextrin.
- Increased number of *H*-bonds formed as the substituted water, returns to the larger pool.
- A reduction of the repulsive interactions between the hydrophobic group of amino acid and the aqueous environment.
- An increase in the hydrophobic-hydrophobic interactions as the inclusion of amino acid takes place into the apolar cavity of cyclodextrin.

3. Experimental

3. 1 Materials

The title compounds *e.g.*, amino acids and cyclodextrins of puriss grade ware bought from Sigma-Aldrich, Germany and used as purchased. The mass fraction purity of *L*-Lys, *L*-Phe, *L*-Glu, α-cyclodextrin and β-cyclodextrin were $\geq$ 0.98, 0.98, 0.99, 0.98, and 0.98 respectively.

3. 2 Apparatus and procedure

Solubility of the chosen cyclodextrins in water (deionized, triply distilled, degassed water with a specific conductance of 1×10^{-6} $S{\cdot}cm^{-1}$) and title compounds *viz.*, amino acids in aqueous cyclodextrin, have been precisely checked to prior of the start of the experimental work, and seen that the selected amino acids freely soluble in all proportion of aq. cyclodextrin. All the stock solutions of the amino acids were prepared by mass (weighed by Mettler Toledo AG-285 with uncertainty 0.0003*g*), and then the working solutions were obtained by mass dilution at 298.15 *K*. The conversions of molality into molarity have been done[14] using density values. Adequate precautions were made to reduce evaporation losses during mixing.

The surface tension experiments were done by platinum ring detachment method using a Tensiometer (K9, KRŰSS; Germany) at the

experimental temperature. The accuracy of the measurement was within ±0.1 $mN{\cdot}m^{-1}$. Temperature of the system has been maintained by circulating auto-thermostated water through a double-wall glass vessel containing the solution.

The densities (ρ) of the solvents were measured by means of vibrating *u*-tube Anton Paar digital density meter (DMA 4500M) with a precision of ±0.00005$g\ cm^{-3}$ maintained at ±0.01K of the desired temperature. It was calibrated by passing deionized, doubly distilled, degassed water and dry air.

The viscosities (η) were measured using a Brookfield DV-III Ultra Programmable Rheometer with fitted spindle size-42. The detail description has already been described earlier.[15]

Refractive index was measured with the help of a Digital Refractometer Mettler Toledo. The light source was LED, λ=589.3nm. The refractometer was calibrated twice using distilled water and calibration was checked after every few measurements. The uncertainty of refractive index measurement was ±0.0002 units.

4. Conclusion

The extensive study concludes the formation of inclusion complexes for all the titled α-amino acids in the apolar cavity of both α and β-cyclodextrin. Surface tension study confirms that 1:1 inclusion complex has been formed. All the derived parameters obtained from the supplementary data of density, viscosity and refractive index strongly support the formation of inclusion complex as well as solute-solvent interaction taking place in the studied solution systems. The order of interaction for selected α-amino acid insight into α- and β-CD is as follows:

L-Glu <L-Lys <L- Phe

Hence, the generous culmination discussed and explained in this exertion exigent the exclusivity of the work and pertinent to the design for sundry applications.

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Figure Captions:

Fig. 1 Plot of surface tension (γ) against concentration of amino acid (m) in w_1=0.000(■), w_1=0.001(♦), w_1=0.003(▲), w_1=0.005(●) mass fraction of α-CD, pure α-CD (×) and in w_2=0.000(□) w_2=0.001(◊), w_2=0.003(Δ), w_2=0.005(○) mass fraction of β–CD, pure β–CD (✱) respectively.

Fig. 2 Plot of limiting molar volume (ϕ_V^0) vs mass fraction for *L*-Lys (brown), *L*-Phe (blue), *L*-Glu (yellow) in aq. α-CD and for *L*-Lys (red), *L*-Phe (green), *L*-Glu (black) in aq. β-CD respectively.

Fig. 3 Plot of viscosity *B*-coefficient vs mass fraction for *L*-Lys (black), *L*-Phe (blue), *L*-Glu (yellow) in aq. α-CD and for *L*-Lys (indigo), *L*-Phe (green), *L*-Glu (red) in aq. β-CD respectively.

Fig. 4 Plot of limiting molar refraction (R_M^0) for selected amino acids in different mass fraction of aq. α- and β-CD respectively.

Figures:

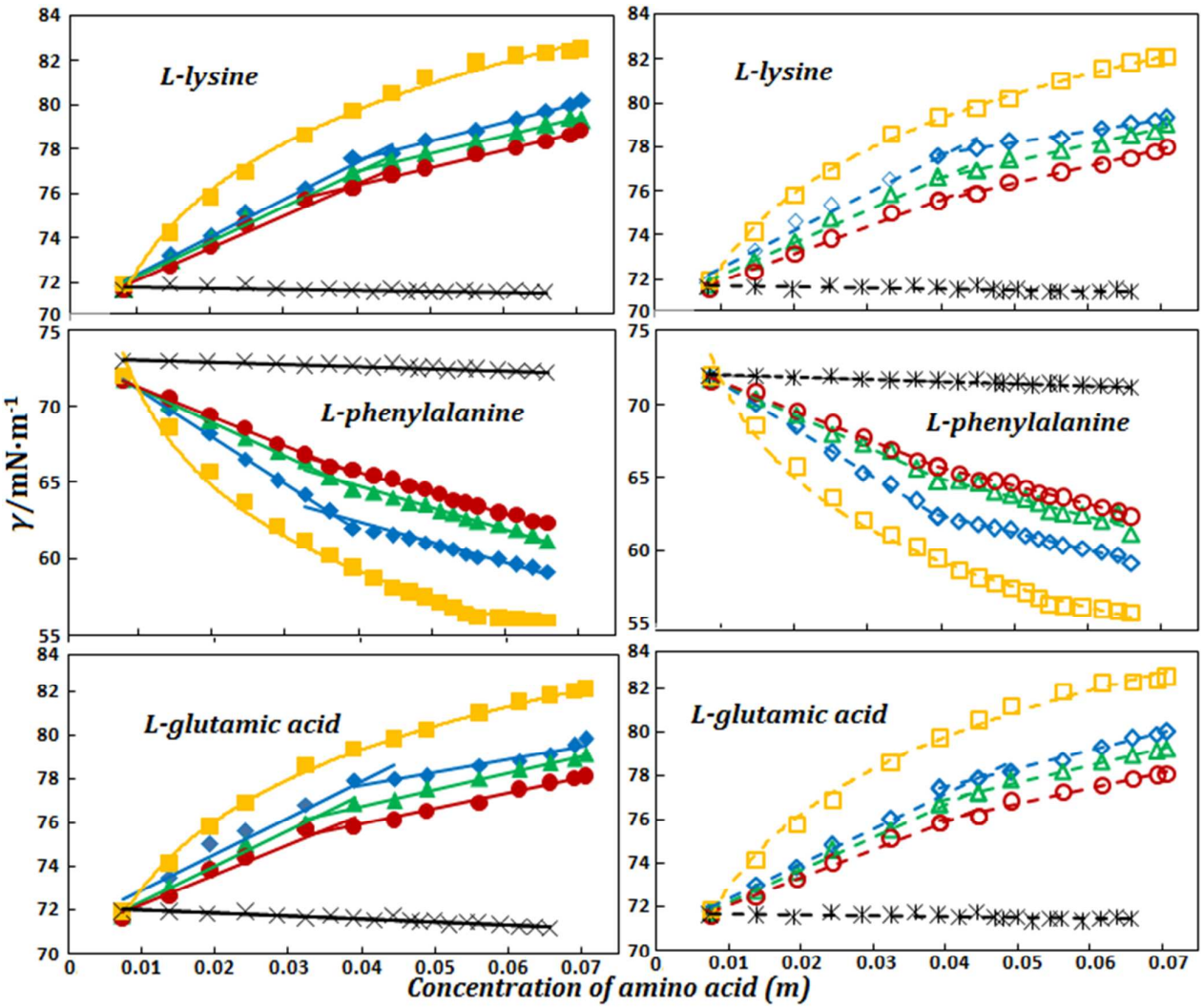


Fig. 1

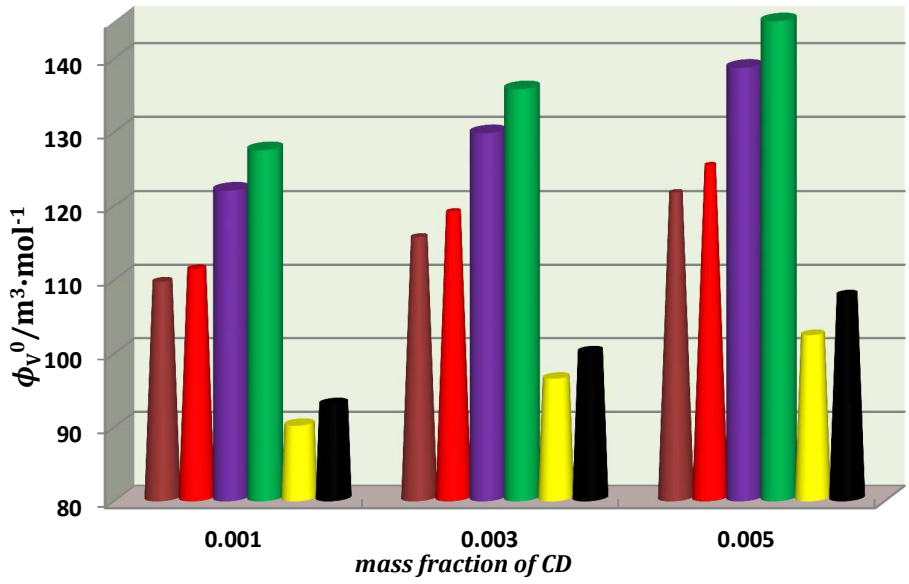


Fig. 2

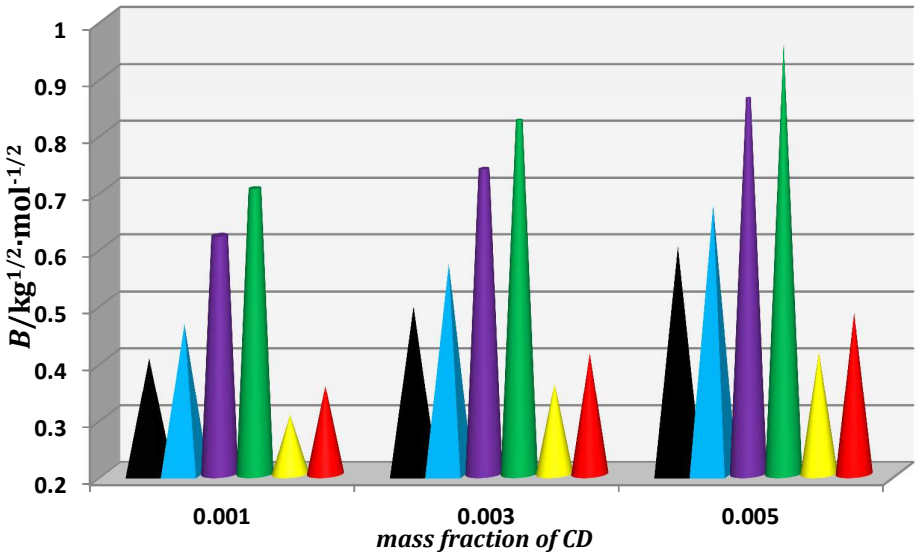


Fig. 3

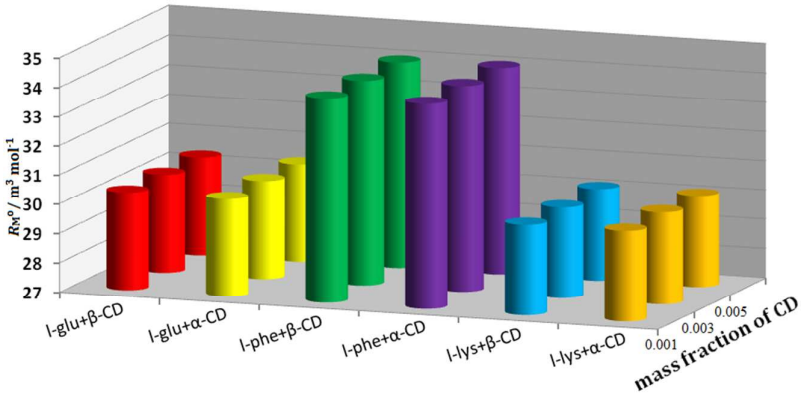


Fig. 4

Scheme legends:

Scheme 1. The molecular structure of chosen α-amino acids and α- and β-cyclodextrin (α- CD 6 membered and β-CD 7 membered sugar ring molecules).

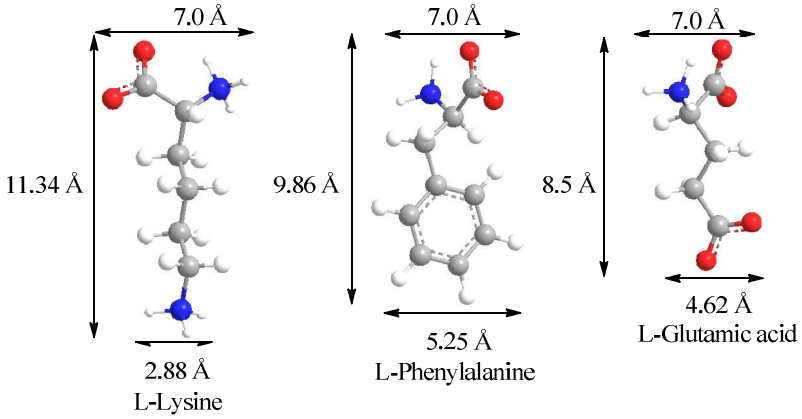
Scheme 2. The plausible stoichiometries inclusion ratio of host:guest molecule.

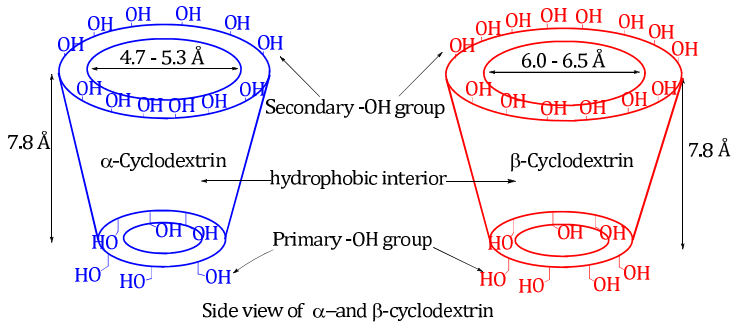
Scheme 3. The feasible and restricted inclusion of host:guest molecule.

Scheme 4. State of amino acids in their respective pH range.

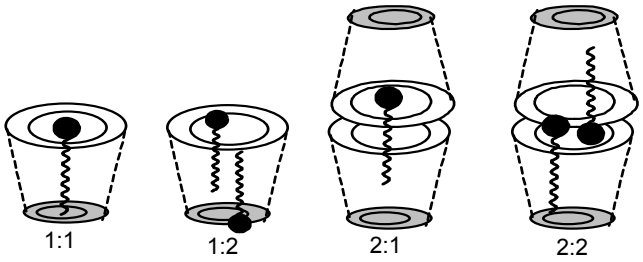
Scheme 5. Schemetic representation of convincing mechanism of 1:1 inclusion complexes insight into α- and β-cyclodextrin with the titled α-amino acids.

Schemes:

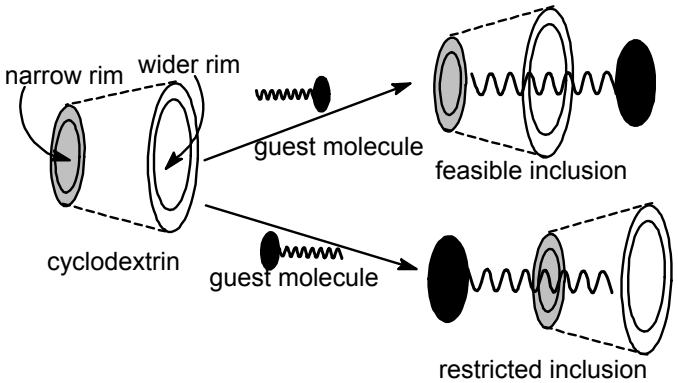




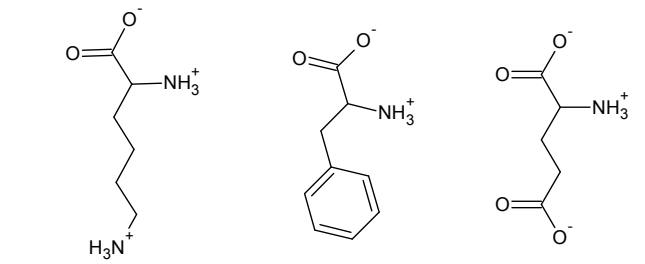
Scheme 1



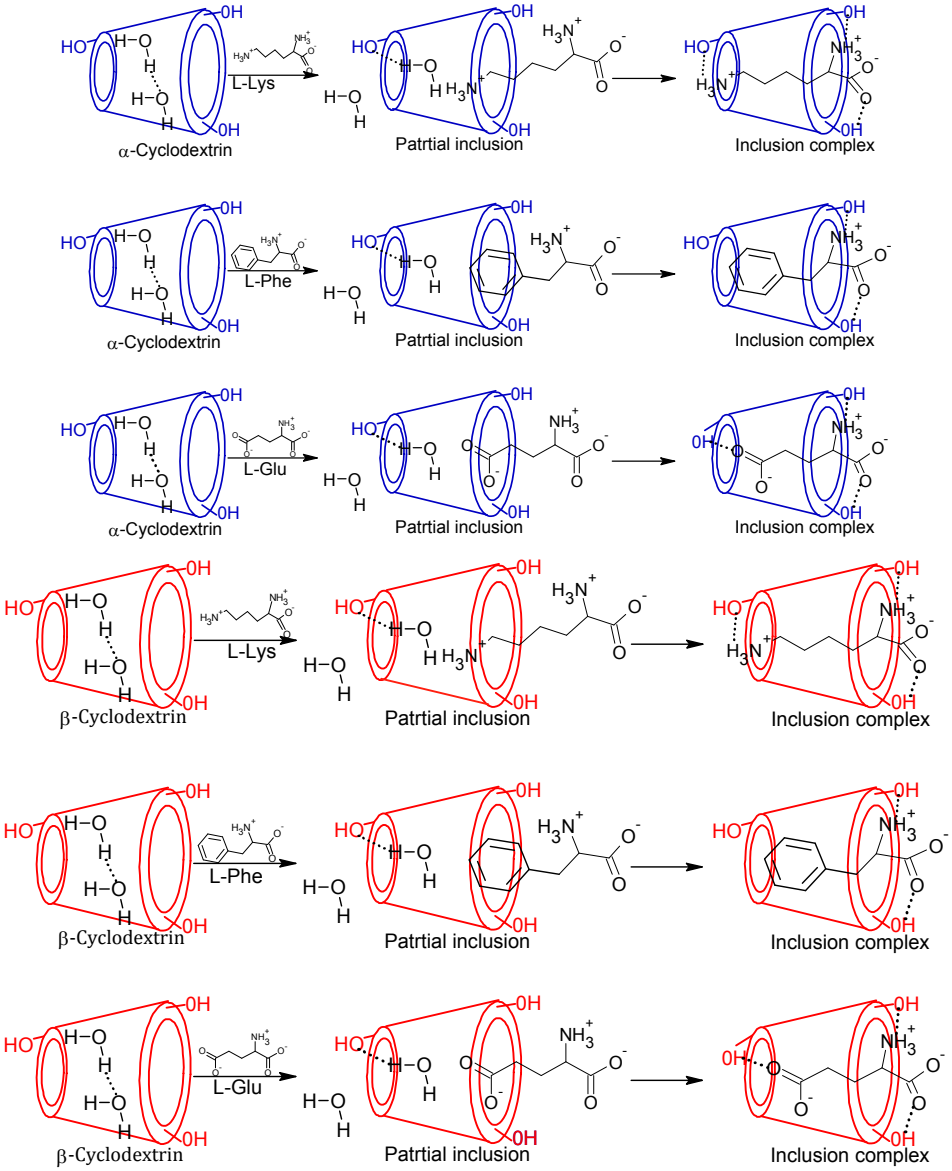
Scheme 2



Scheme 3



Scheme 4



Scheme 5

Tables:

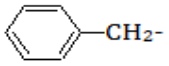
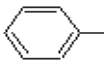
Table 1. Values of surface tension at the break point (γ) with corresponding concentration of amino acids in different mass fraction of aqueous α and β-cyclodextrin respectively at 298.15K[a]

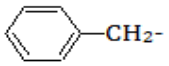
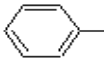
mass fraction (w)	conc (m)	γ /mNm^{-1}	conc (m)	γ/mNm^{-1}	conc (m)	γ/mNm^{-1}
	L-Lys		*L*-Phe		*L*-Glu	
w_1=0.001[b]	0.0441	77.81	0.0389	62.37	0.0403	77.67
w_1=0.003[b]	0.0427	77.11	0.0385	65.06	0.0396	76.62
w_1=0.005[b]	0.0421	76.26	0.0378	65.66	0.0389	75.56
w_2=0.001[b]	0.0413	77.67	0.0364	62.83	0.0387	77.61
w_2=0.003[b]	0.0405	77.06	0.0356	65.24	0.0361	76.29
w_2=0.005[b]	0.0381	76.15	0.0341	66.22	0.0337	75.49

[a] Standard uncertainties u are: $u(T)$ =0.01K

[b] w_1 and w_2 are mass fractions of α- and β-cyclodextrin in aqueous mixture respectively

Table 2. Contributions of zwitter ionic group (NH_3^+, COO^-), CH_2 group, end group and the other alkyl chains to the limiting apparent molar volume, ϕ_V^0, and viscosity B-coefficient for amino acids in different mass fraction of aqueous α and β-cyclodextrin respectively at 298.15K[a]

Groups	ϕ_V^0 /m^3 mol^{-1}			B/$kg^{1/2}\cdot mol^{-1/2}$		
	w_1=0.001[b]	w_1=0.003[b]	w_1=0.005[b]	w_1=0.001[b]	w_1=0.003[b]	w_1=0.005[b]
L-Lys						
NH_3^+, COO^-	27.57	25.99	24.24	0.098	0.068	0.032
-CH_2-	14.71	16.66	18.71	0.037	0.069	0.107
-$(CH_2)_4NH_2$	67.25	72.81	78.61	0.268	0.356	0.460
end –NH_2 gr	8.41	6.17	3.77	0.120	0.080	0.032
L-Phe						
NH_3^+, COO^-	30.16	28.59	26.58	0.052	0.108	0.168
-CH_2-	12.12	14.06	16.37	0.083	0.029	-0.029
	79.87	87.21	95.82	0.484	0.600	0.665
	67.75	73.15	79.45	0.401	0.571	0.636
L-Glu						
NH_3^+, COO^-	34.94	33.23	31.61	0.107	0.082	0.056
-CH_2-	7.34	9.42	11.34	0.028	0.055	0.083

-$(CH_2)_2COOH$	47.82	53.84	59.33	0.168	0.222	0.276
end -*COOH*	33.14	35.00	36.65	0.112	0.112	0.110
	w_2=0.001[b]	w_2=0.003[b]	w_2=0.005[b]	w_2=0.001[b]	w_2=0.003[b]	w_2=0.005[b]
L-Lys						
NH_3^+, COO^-	27.13	24.98	23.11	0.079	0.044	0.010
-CH_2-	15.37	17.94	20.11	0.058	0.096	0.133
-$(CH_2)_4NH_2$	68.73	75.92	82.02	0.235	0.428	0.528
end –NH_2 gr	7.25	4.16	1.58	0.093	0.044	-0.004
L-Phe						
NH_3^+, COO^-	28.83	27.12	24.76	0.094	0.151	0.218
-CH_2-	13.67	15.80	18.46	0.041	-0.014	-0.079
	85.07	92.97	102.87	0.568	0.657	0.663
	71.40	77.17	84.41	0.527	0.643	0.584
L-Glu						
NH_3^+, COO^-	34.06	33.16	29.85	0.081	0.055	0.023
-CH_2-	8.44	9.76	13.37	0.054	0.082	0.116
-$(CH_2)_2COOH$	50.54	57.14	64.57	0.220	0.275	0.343
end -*COOH*	33.66	37.62	37.83	0.112	0.111	0.111

[a] Standard uncertainties *u* are: $u(T)$ =0.01*K*

[b] w_1 and w_2 are mass fractions of *α*- and *β*-cyclodextrin in aqueous mixture respectively

Table 3. Hydration number (n_H), and solvation number (S_n) of chosen amino acids in deferent mass fraction of different mass fraction of aqueous *α* and *β*-cyclodextrin respectively at 298.15*K*[a]

	n_H			S_n		
Aq. *α*-CD (w_1)[b]	0.001	0.003	0.005	0.001	0.003	0.005
L-Lys	6.98	5.01	2.97	3.68	4.27	4.93
L-Phe	5.52	2.95	-0.02	5.07	5.68	6.21
L-Glu	4.54	2.41	0.48	3.36	3.72	4.06
Aq. *β* -CD (w_2)[b]						
L-Lys	6.42	3.88	1.75	4.15	4.78	5.36
L-Phe	3.71	0.94	-2.46	5.51	6.05	6.57
L-Glu	3.56	1.22	-1.35	3.82	4.12	4.47

[a] Standard uncertainties *u* are: $u(T)$ =0.01*K*

[b] w_1 and w_2 are mass fractions of *α*- and *β*-cyclodextrin in aqueous mixture respectively

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