Electronic Supplementary Information

Potassium caffeate/caffeic acid co-crystal: the rat race between cathecolic and carboxylic moiety in an atypical hybrid co-crystal

Giuseppe M. Lombardo[a], Gustavo Portalone[b], Ugo Chiacchio[a], Antonio Rescifina[a*] and Francesco Punzo[a*]

[a] *Dipartimento di Scienze del Farmaco, Università degli Studi di Catania, Viale Andrea Doria 6, 95125, Catania, Italy*

[b] *Dipartimento di Chimica , "Sapienza" Università degli Studi di Roma, P.le A. Moro 5, 00185, Roma, Italy*

X-ray single crystal data:

$C_{18}H_{15}KO_8 \cdot H_2O$, M_r = 416,42 triclinic, P-1, a = 9.7482(7) Å, b = 10.2754(9) Å, c = 10.5529(9) Å , α = 114.473(8)°, β = 108.182(7)°, γ = 95.313(7)°, V = 883.45(16) (Å^3), Z = 2, ρ = 1.565 mg M^{-3}, μ = 0.353 mm^{-1}, λ = 0.71069 Å, T = 298(2) K, $F(000)$ = 432, crystal size = 0.20 × 0.15 × 0.12 mm, 6402 reflections collected, 3084 reflections unique (R_{int} = 0.032), GoF = 1.037, $R[F^2 > 2\sigma(F^2)]$ = 0.051, $wR(F^2)$ = 0.121, min/max residual density = -0.25/0.34 e Å^{-3}. Completeness to θ (25.1°) = 0.985.

Table ST1 Molecular Dynamics Average values and estimated standard deviations (e.s.d.) attained by Model I and II from NPT simulation at 293 K of the Total, Potential and Kinetic Energies (*kcal mol*$^{-1}$), and Shannon Entropy for and relative differences Δ = E(**II**) - E(**I**)

	Model **I**		Model **II**		Δ	
		e.s.d.		e.s.d.		e.s.d.
E_{Tot}	-7052.350	4.769	-7094.935	4.706	-42.585	6.700
E_{Pot}	-7679.954	14.115	-7722.556	14.099	-42.602	19.950
E_{Kin}	627.604	13.641	627.621	13.652	0.015	19.299
Entropy	1467.53	360.83	1390.82	372.79	-76.72	518.68

Table ST2 Estimated standard deviation (e.s.d.) of the adps of model I and II with respect to X-ray ones

	C1 → O4	H2 → H41	C1A → O4A	H2A → H4A1	H_2O	K
Model **I**	0.0123	0.0284	0.0073	0.0239	0.0259	0.0162
Model **II**	0.0166	0.0283	0.0139	0.0157	0.0366	0.0275

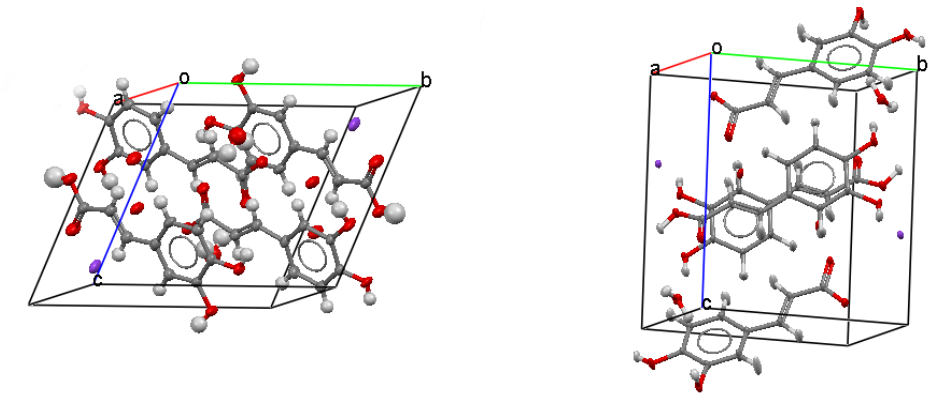

Fig. SF1 X-ray structure (left) and model **II** one (right) unit cell.

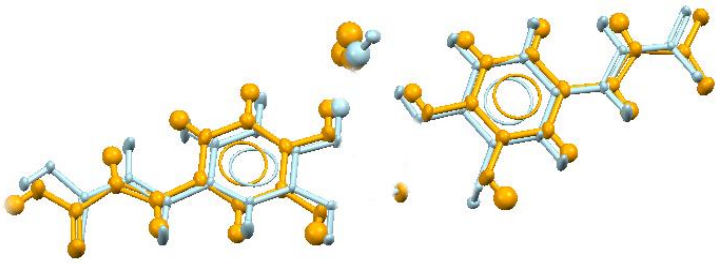

Figure SF2 Superimposition of the asymmetric unit of the X-ray structure (orange) and model **II** (light blue). The position of the K ion is coincident and therefore resulted eclipsed.

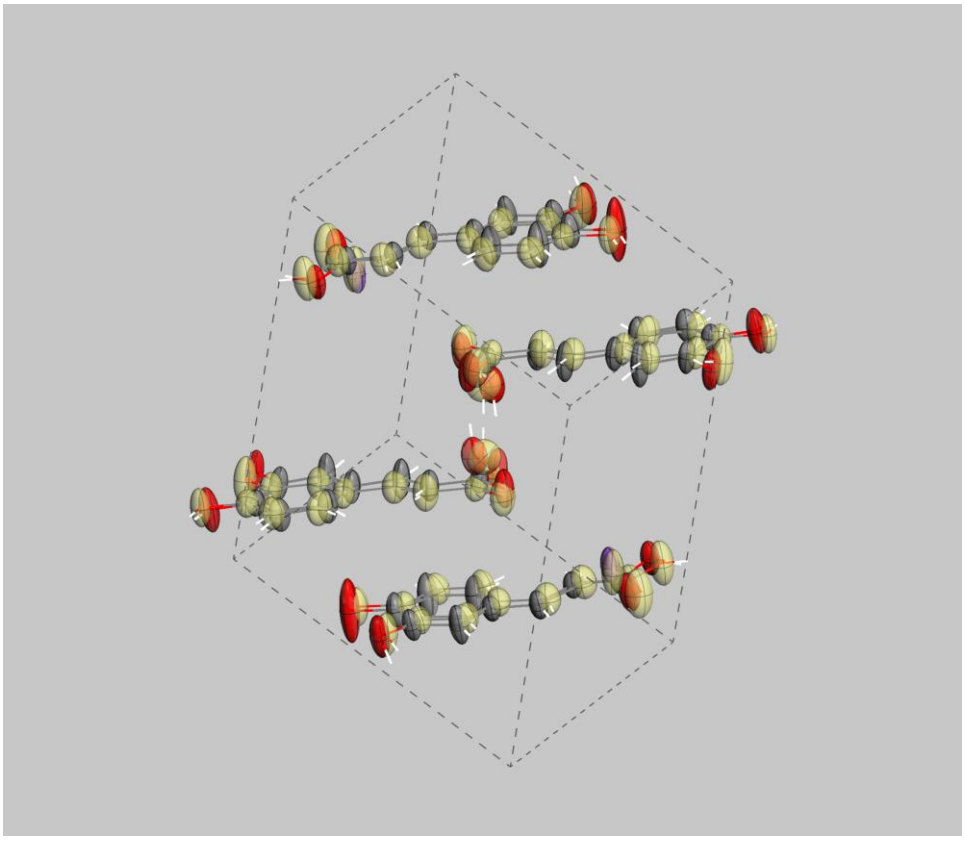

Figure SF3 Superimposition of the experimental crystal packing with the model I MD averaged one. The experimental anisotropic thermal factors are shown (yellowish) and compared with the MD calculated ones (in red and gray for oxygen and carbons, respectively). The agreement in the anisotropic thermal factors is extended to the whole MD calculated super-cell and not only confined to the single unit fragment.

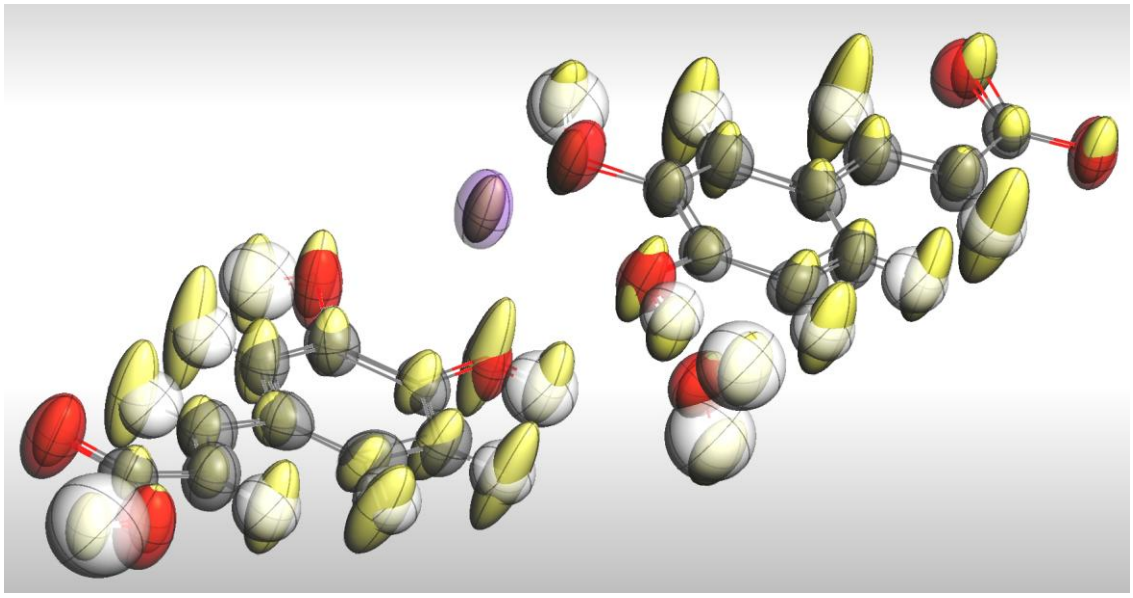

Figure SF4 Superimposition of the whole asymmetric units (with displayed hydrogens, at difference with Figure 6 in the text) with the MD averaged ones of model I MD. The experimental anisotropic thermal factors are shown (in red and gray for oxygen and carbons, respectively) and compared with the MD calculated ones (yellowish).

Structure II CIF

```
data_II
_audit_creation_date              2011-07-30
_audit_creation_method            ' '
_symmetry_space_group_name_H-M    'P-1'
_symmetry_Int_Tables_number       2
_symmetry_cell_setting            triclinic
loop_
_symmetry_equiv_pos_as_xyz
  x,y,z
  -x,-y,-z
_cell_length_a                    8.1277
_cell_length_b                    10.1980
_cell_length_c                    10.6385
_cell_angle_alpha                 85.8454
_cell_angle_beta                  80.3161
_cell_angle_gamma                 74.8444
loop_
_atom_site_label
_atom_site_type_symbol
_atom_site_fract_x
_atom_site_fract_y
_atom_site_fract_z
_atom_site_U_iso_or_equiv
_atom_site_adp_type
_atom_site_occupancy
K      K     0.14294  -0.01203   0.63554   0.01276  Uani   1.00
O1     O     0.62213  -0.09471  -0.68739   0.02045  Uani   1.00
O2     O     0.35784  -0.04405  -0.57173   0.01815  Uani   1.00
H21    H     0.34542   0.02748  -0.63868   0.02069  Uani   1.00
O3     O     0.99943  -0.83678  -0.53750   0.01598  Uani   1.00
H31    H     1.09519  -0.81291  -0.59510   0.01925  Uani   1.00
O4     O     0.88336  -0.83724  -0.28464   0.02069  Uani   1.00
H41    H     0.79158  -0.85815  -0.21989   0.02075  Uani   1.00
C1     C     0.51525  -0.12811  -0.60556   0.01330  Uani   1.00
C2     C     0.55310  -0.25630  -0.53665   0.01483  Uani   1.00
```

```
H2      H      0.46652  -0.26484  -0.45321   0.04245  Uani   1.00
C3      C      0.68902  -0.35981  -0.57602   0.01744  Uani   1.00
H3      H      0.76477  -0.34236  -0.66417   0.04622  Uani   1.00
C4      C      0.72533  -0.48572  -0.50216   0.01417  Uani   1.00
C5      C      0.83999  -0.60203  -0.55859   0.01624  Uani   1.00
H5      H      0.88813  -0.60021  -0.65789   0.03273  Uani   1.00
C6      C      0.88996  -0.72113  -0.48497   0.01222  Uani   1.00
C7      C      0.81952  -0.72618  -0.35580   0.01232  Uani   1.00
C8      C      0.69776  -0.61485  -0.30088   0.01687  Uani   1.00
H8      H      0.64480  -0.62188  -0.20247   0.03129  Uani   1.00
C9      C      0.65155  -0.49497  -0.37360   0.02001  Uani   1.00
H9      H      0.56418  -0.41040  -0.32673   0.04613  Uani   1.00
O1A     O      0.44359   0.15090   0.12166   0.01512  Uani   1.00
O2A     O      0.26171   0.17515   0.29475   0.02264  Uani   1.00
O3A     O      0.32043   0.80445  -0.23990   0.01526  Uani   1.00
H3A1    H      0.39215   0.84668  -0.19815   0.01932  Uani   1.00
O4A     O      0.01191   0.94793  -0.13426   0.02308  Uani   1.00
H4A1    H     -0.10905   0.98617  -0.10000   0.02109  Uani   1.00
C1A     C      0.31434   0.22076   0.18888   0.01269  Uani   1.00
C2A     C      0.23139   0.35684   0.14966   0.01472  Uani   1.00
H2A     H      0.12589   0.41005   0.21375   0.03839  Uani   1.00
C3A     C      0.28696   0.41543   0.03904   0.01579  Uani   1.00
H3A     H      0.39552   0.35309  -0.01880   0.03725  Uani   1.00
C4A     C      0.20775   0.55381   0.00237   0.01396  Uani   1.00
C5A     C      0.29399   0.61163  -0.10268   0.02234  Uani   1.00
H5A     H      0.41313   0.55468  -0.14931   0.05212  Uani   1.00
C6A     C      0.22826   0.74474  -0.14432   0.01356  Uani   1.00
C7A     C      0.07106   0.82197  -0.08360   0.01177  Uani   1.00
C8A     C     -0.01573   0.76810   0.02420   0.01513  Uani   1.00
H8A     H     -0.13299   0.82880   0.07426   0.03114  Uani   1.00
C9A     C      0.05171   0.63389   0.06650   0.01553  Uani   1.00
H9A     H     -0.02193   0.59595   0.14621   0.03359  Uani   1.00
O5      O      0.67563   0.07261  -0.09641   0.01753  Uani   1.00
H52     H      0.62393   0.00165  -0.11729   0.02296  Uani   1.00
H51     H      0.59558   0.10644  -0.01963   0.02185  Uani   1.00
loop_
_atom_site_aniso_label
_atom_site_aniso_U_11
_atom_site_aniso_U_22
_atom_site_aniso_U_33
_atom_site_aniso_U_12
_atom_site_aniso_U_13
_atom_site_aniso_U_23
K          0.01205   0.01053   0.01252   0.00110  -0.00015   0.00169
O1         0.01640   0.01662   0.02478  -0.00337   0.00298   0.00506
O2         0.01637   0.01447   0.01684   0.00339   0.00217   0.00556
H21        0.02037   0.01493   0.01919   0.00347   0.00241   0.00670
O3         0.01581   0.00943   0.01766   0.00034   0.00597  -0.00067
H31        0.01632   0.01447   0.02026   0.00097   0.00741   0.00127
O4         0.01749   0.01622   0.01811   0.00671   0.00533   0.00681
H41        0.02073   0.01544   0.01885   0.00150   0.00517   0.00492
C1         0.01277   0.00996   0.01480  -0.00049  -0.00027   0.00181
C2         0.01381   0.01118   0.01554   0.00136   0.00028   0.00273
H2         0.03863   0.03030   0.03228   0.01740   0.01800   0.01794
C3         0.01978   0.01115   0.01542   0.00283   0.00226   0.00197
H3         0.05445   0.02489   0.03174   0.01587   0.02360   0.01218
C4         0.01625   0.00983   0.01225   0.00229   0.00038   0.00016
C5         0.01880   0.01093   0.01305   0.00262   0.00342   0.00094
H5         0.04224   0.02226   0.01805   0.00776   0.01170   0.00419
C6         0.01191   0.00866   0.01284   0.00037   0.00233  -0.00013
C7         0.01132   0.00996   0.01199   0.00171   0.00105   0.00072
C8         0.02012   0.01323   0.01049   0.00549   0.00101  -0.00007
H8         0.04058   0.02446   0.01288   0.01258   0.00612   0.00234
```

```
C9          0.02653   0.01304   0.01144   0.00780   0.00179  -0.00019
H9          0.06738   0.02466   0.01778   0.02625   0.01143   0.00310
O1A         0.01508   0.01158   0.01526  -0.00051   0.00236   0.00044
O2A         0.02148   0.01473   0.02100   0.00411   0.00893   0.00863
O3A         0.01190   0.01431   0.01578   0.00006   0.00081   0.00494
H3A1        0.01363   0.01969   0.02260  -0.00305  -0.00094   0.00402
O4A         0.01942   0.01657   0.02180   0.00683   0.00668   0.00881
H4A1        0.01744   0.01475   0.02284   0.00482   0.00401   0.00365
C1A         0.01167   0.00961   0.01405  -0.00081   0.00128   0.00296
C2A         0.01304   0.01091   0.01678  -0.00049   0.00107   0.00464
H2A         0.03258   0.02355   0.03722   0.01182   0.01873   0.01501
C3A         0.01709   0.01080   0.01537   0.00010   0.00127   0.00403
H3A         0.04188   0.02034   0.02882   0.01155   0.01685   0.01019
C4A         0.01322   0.01059   0.01489  -0.00029   0.00066   0.00369
C5A         0.01824   0.01410   0.02392   0.00503   0.00830   0.00881
H5A         0.03974   0.02835   0.05458   0.01968   0.03134   0.02347
C6A         0.01118   0.01121   0.01456   0.00078   0.00095   0.00377
C7A         0.01081   0.01018   0.01199   0.00015  -0.00059   0.00162
C8A         0.01336   0.01300   0.01480   0.00064   0.00200   0.00261
H8A         0.02504   0.02314   0.03003   0.00779   0.01294   0.00673
C9A         0.01387   0.01312   0.01574  -0.00041   0.00183   0.00391
H9A         0.02765   0.02468   0.03289   0.00471   0.01445   0.01389
O5          0.01431   0.01547   0.02013  -0.00331   0.00387   0.00002
H52         0.02205   0.02068   0.02562  -0.00790   0.00275  -0.00315
H51         0.01963   0.02075   0.02178  -0.00377   0.00520  -0.00326
loop_
_geom_bond_atom_site_label_1
_geom_bond_atom_site_label_2
_geom_bond_distance
_geom_bond_site_symmetry_2
_geom_bond_publ_flag
O1      C1      1.219   .      ?
O2      H21     0.980   .      ?
O2      C1      1.348   .      ?
O3      H31     0.979   .      ?
O3      C6      1.369   .      ?
O4      H41     0.983   .      ?
O4      C7      1.351   .      ?
C1      C2      1.438   .      ?
C2      H2      1.049   .      ?
C2      C3      1.345   .      ?
C3      H3      1.063   .      ?
C3      C4      1.445   .      ?
C4      C5      1.405   .      ?
C4      C9      1.405   .      ?
C5      H5      1.064   .      ?
C5      C6      1.402   .      ?
C6      C7      1.400   .      ?
C7      C8      1.387   .      ?
C8      H8      1.068   .      ?
C8      C9      1.398   .      ?
C9      H9      1.058   .      ?
O1A     C1A     1.246   .      ?
O2A     C1A     1.239   .      ?
O3A     H3A1    0.984   .      ?
O3A     C6A     1.363   .      ?
O4A     H4A1    0.975   .      ?
O4A     C7A     1.355   .      ?
C1A     C2A     1.441   .      ?
C2A     H2A     1.053   .      ?
C2A     C3A     1.344   .      ?
C3A     H3A     1.069   .      ?
C3A     C4A     1.445   .      ?
```

C4A	C5A	1.395	.	?
C4A	C9A	1.410	.	?
C5A	H5A	1.052	.	?
C5A	C6A	1.392	.	?
C6A	C7A	1.393	.	?
C7A	C8A	1.398	.	?
C8A	H8A	1.069	.	?
C8A	C9A	1.406	.	?
C9A	H9A	1.063	.	?
O5	H52	0.981	.	?
O5	H51	0.977	.	?