Supporting Information For

Exploration and investigation of various solid forms of an anti-glaucoma drug - Dichlorphenamide

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[1]Ananya Kar and Lopamudra Giri contributed equally to this work as first authors.

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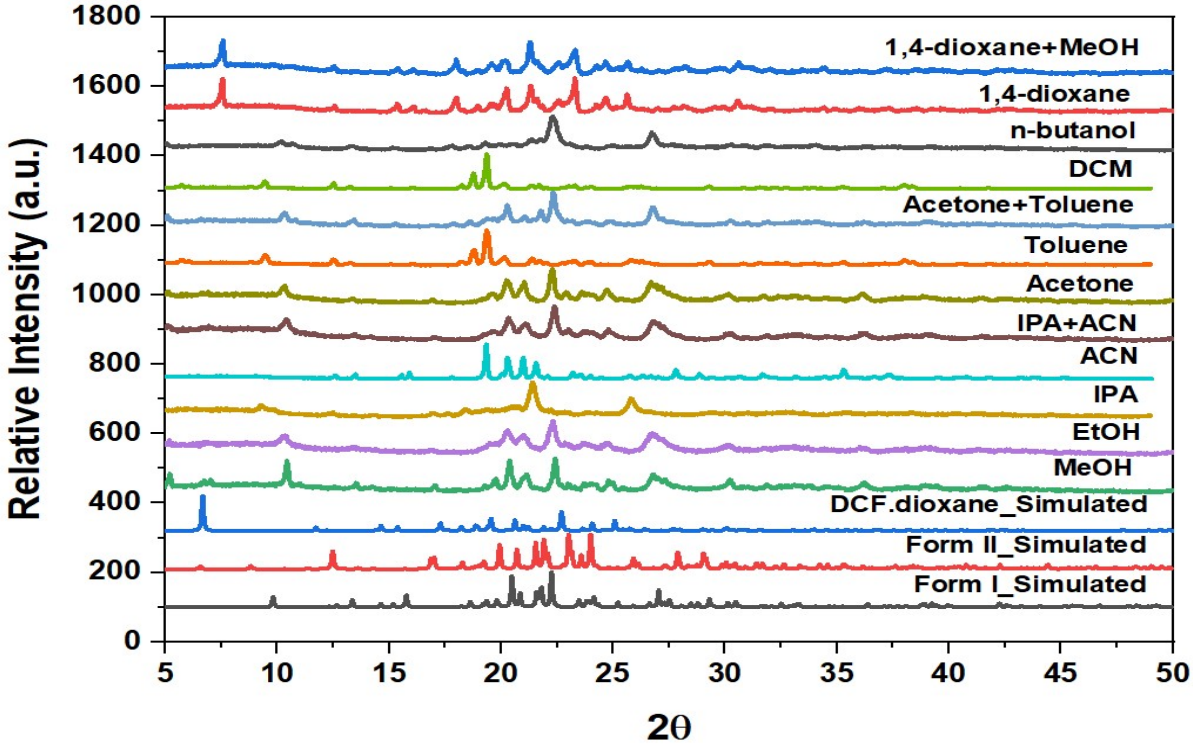
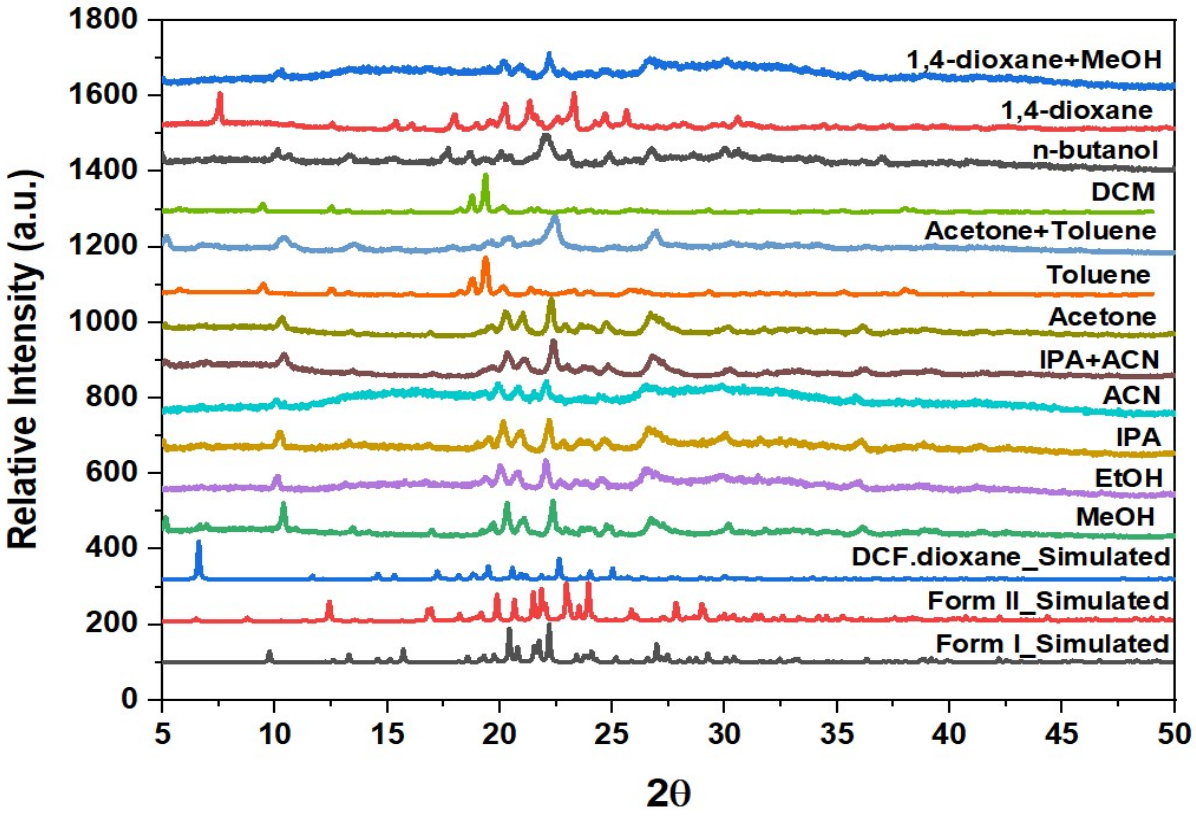
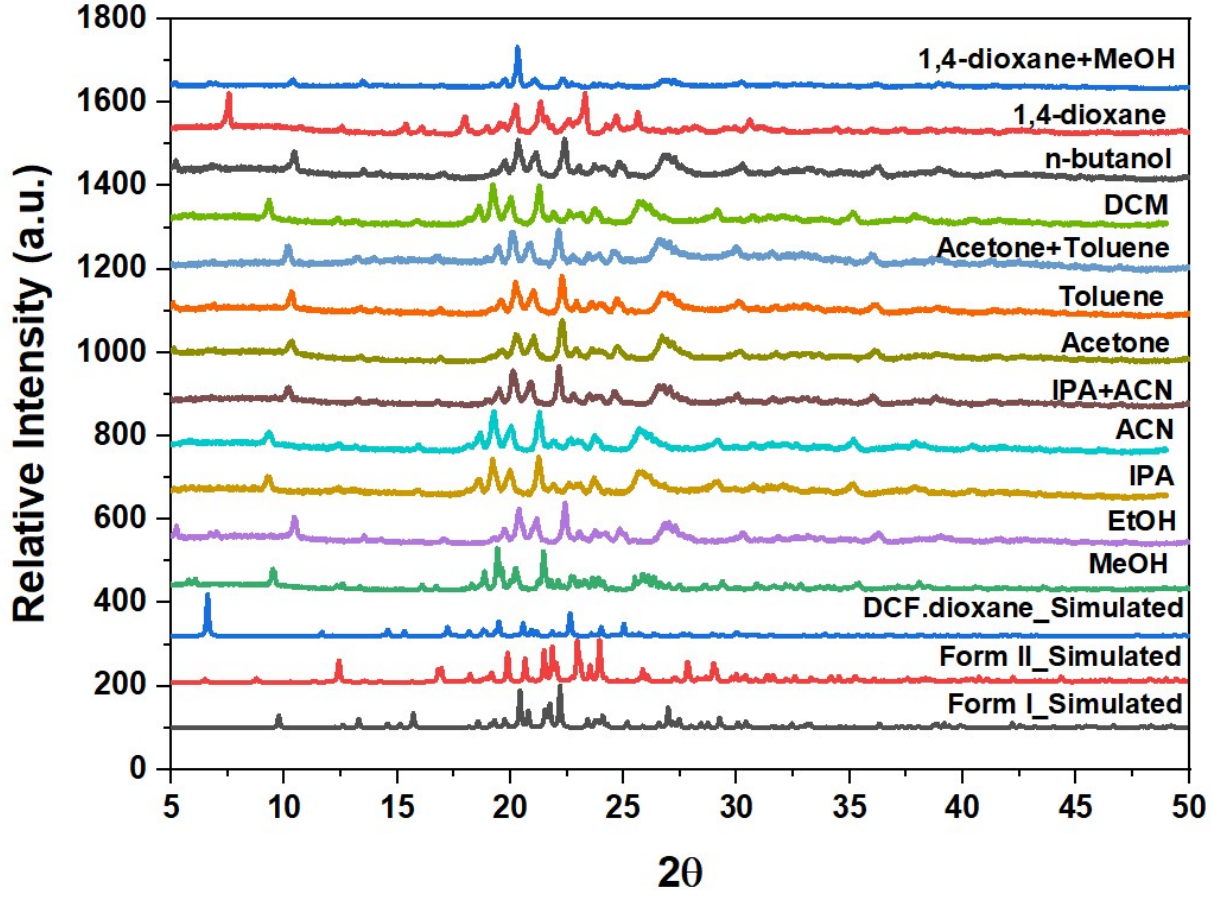

Relative Intensity (a.u.)
2θ
1,4-dioxane+MeOH
1,4-dioxane
n-butanol
DCM
Acetone+Toluene
Toluene
Acetone
IPA+ACN
ACN
IPA
EtOH
MeOH
DCF.dioxane_Simulated
Form II_Simulated
Form I_Simulated

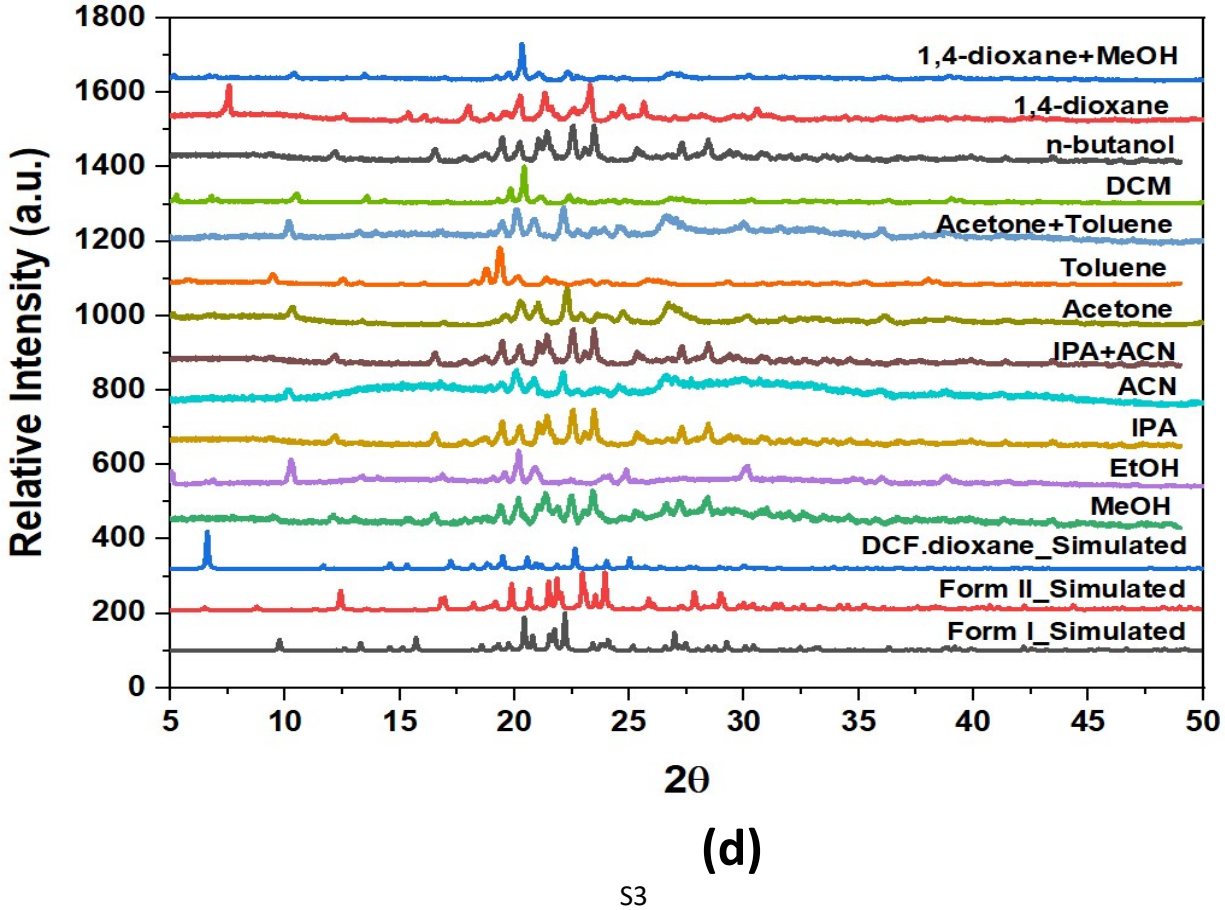
(a)


Relative Intensity (a.u.)
2θ
1,4-dioxane+MeOH
1,4-dioxane
n-butanol
DCM
Acetone+Toluene
Toluene
Acetone
IPA+ACN
ACN
IPA
EtOH
MeOH
DCF.dioxane_Simulated
Form II_Simulated
Form I_Simulated

(b)


Relative Intensity (a.u.)
2θ
1,4-dioxane+MeOH
1,4-dioxane
n-butanol
DCM
Acetone+Toluene
Toluene
Acetone
IPA+ACN
ACN
IPA
EtOH
MeOH
DCF.dioxane_Simulated
Form II_Simulated
Form I_Simulated

(c)


Relative Intensity (a.u.)
2θ
1,4-dioxane+MeOH
1,4-dioxane
n-butanol
DCM
Acetone+Toluene
Toluene
Acetone
IPA+ACN
ACN
IPA
EtOH
MeOH
DCF.dioxane_Simulated
Form II_Simulated
Form I_Simulated

(d)

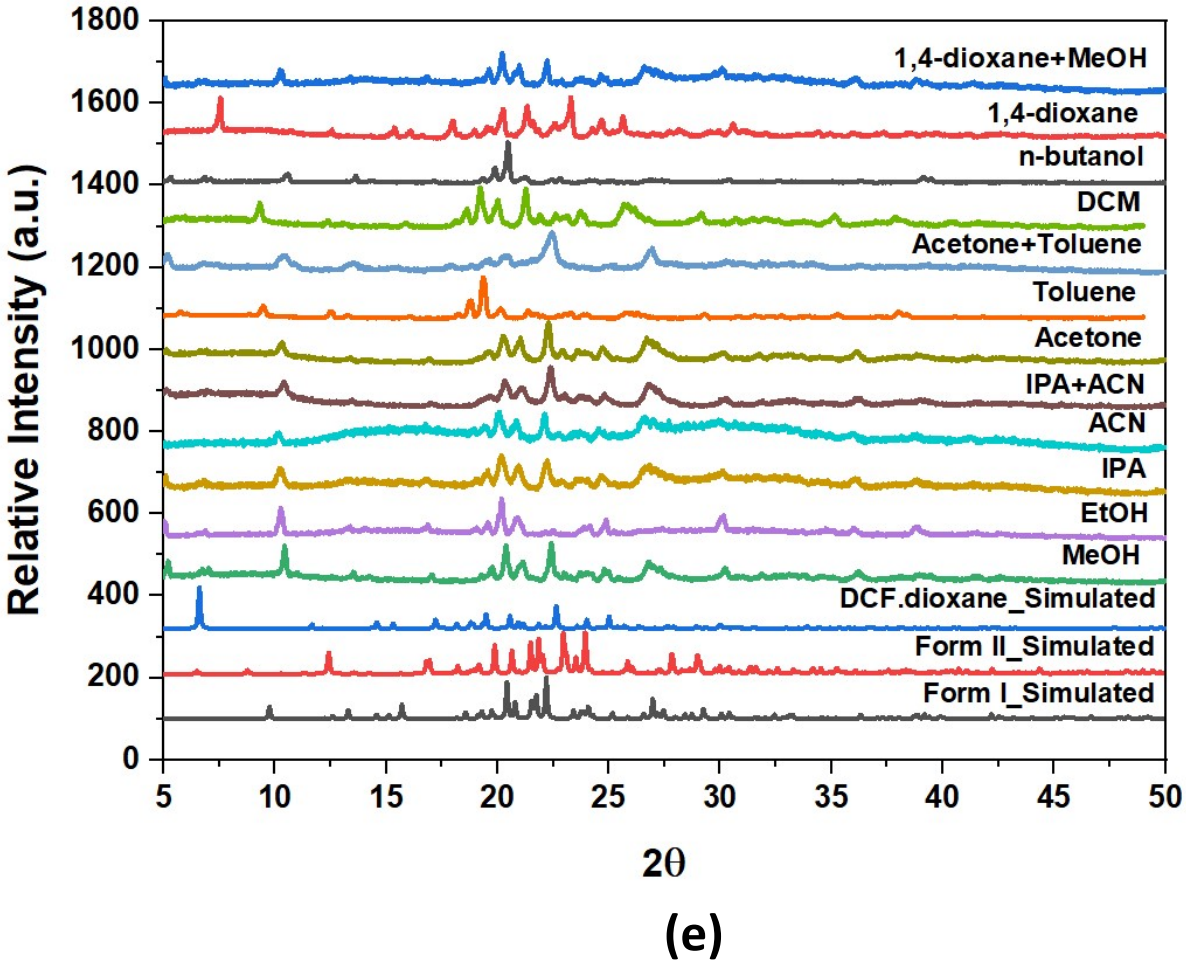
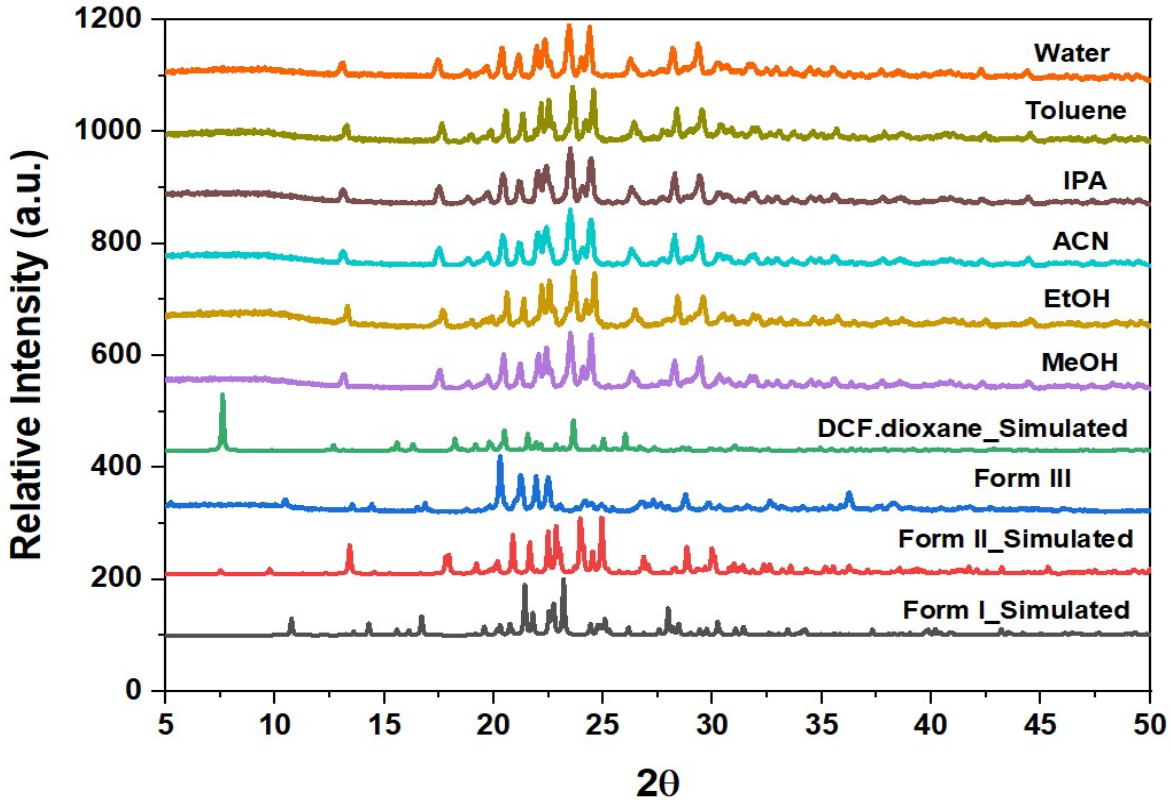


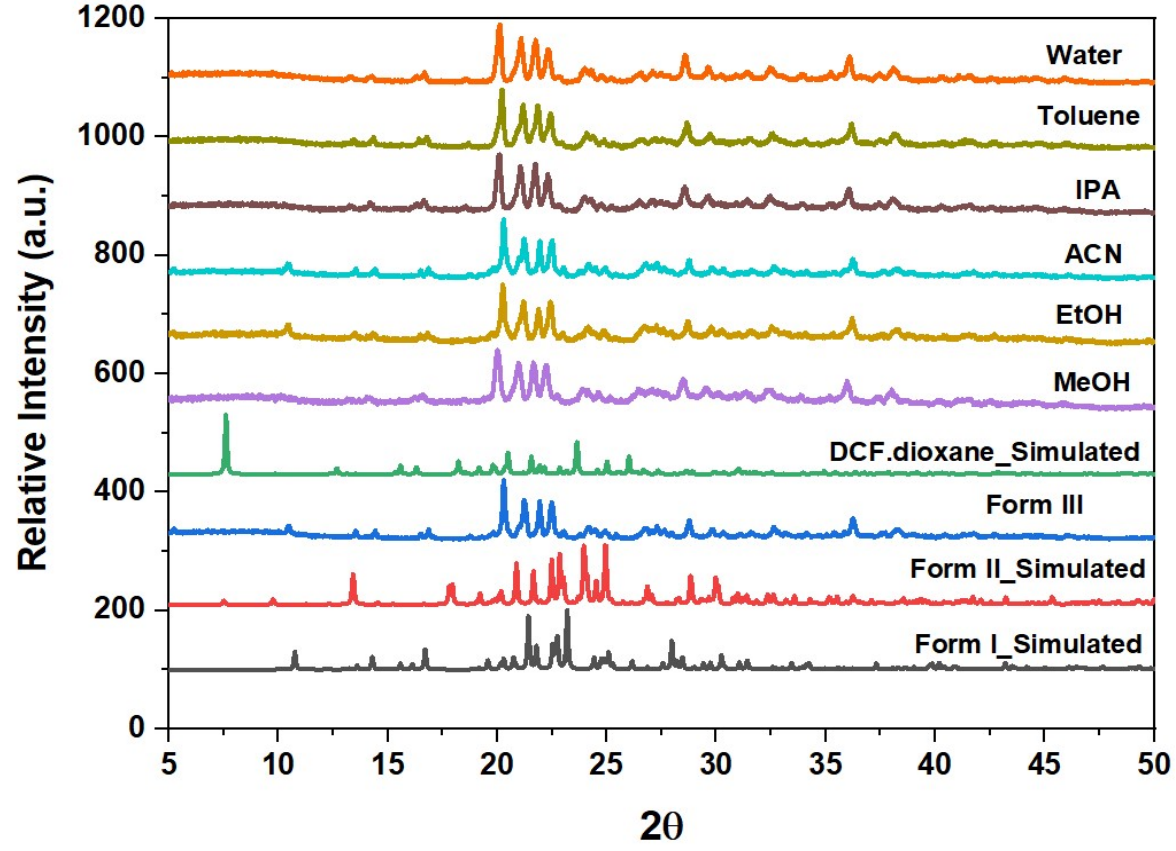
Figure S1. Depiction of the emergence of different forms under various reaction conditions (a) rotary evaporation, (b) hot-melt extrusion, (c) liquid-assisted grinding (LAG) (d) LAG followed by slow-evaporation and (e) sonication.

Table S1. Hydrogen bond distances (Å) and angles (°) of various forms of DCF.

Solid forms	*D*–H···*A* (Å)	*D*–H(Å)	H···*A*(Å)	*D*–*A*(Å)	*D*–H···*A*(Å)	Symmetry
Form I	N2−H4···O4	0.860	2.15	2.980(1)	162	1/2-x, -1/2+y, 1/2-z
	N1−H6···O1	0.860	2.16	2.903(1)	145	-1/2+x, -1/2+y, z
	N2−H3···O3	0.860	2.36	2.985(1)	129	-1/2+x, 1/2+y, z
	N1−H5···O2	0.859	2.93	2.931(1)	123	1/2-x, -1/2+y, 1/2-z
	C3−H2···O3	1.066	3.53	3.536(1)	161	1-x, 1-y, 1-z
Form II	N4−H7···O4	0.851	2.03	2.881(1)	174	-1+x, y, z
	N1−H8···O6	0.759	2.25	2.972(1)	160	-x, -1/2+y, 1/2-z
	N4−H3···O8	0.801	2.30	3.051(2)	157	1-x, -1/2+y, 1/2-z
	N2−H10···O2	0.773	2.40	3.171(1)	174	-x, -1/2+y, 1/2-z
DCF.dioxane	N1−H1A···O6	0.890	1.95	2.833(1)	167	x, y, z
	N2−H2C···O5	0.890	2.02	2.880(3)	162	1-x, 1-y, 2-z
	N1−H1B···O4	0.890	2.58	3.342(1)	144	1-x, -y, 1-z


Relative Intensity (a.u.)
2θ
Water
Toluene
IPA
ACN
EtOH
MeOH
DCF.dioxane_Simulated
Form III
Form II_Simulated
Form I_Simulated

(a)


Relative Intensity (a.u.)
2θ
Water
Toluene
IPA
ACN
EtOH
MeOH
DCF.dioxane_Simulated
Form III
Form II_Simulated
Form I_Simulated

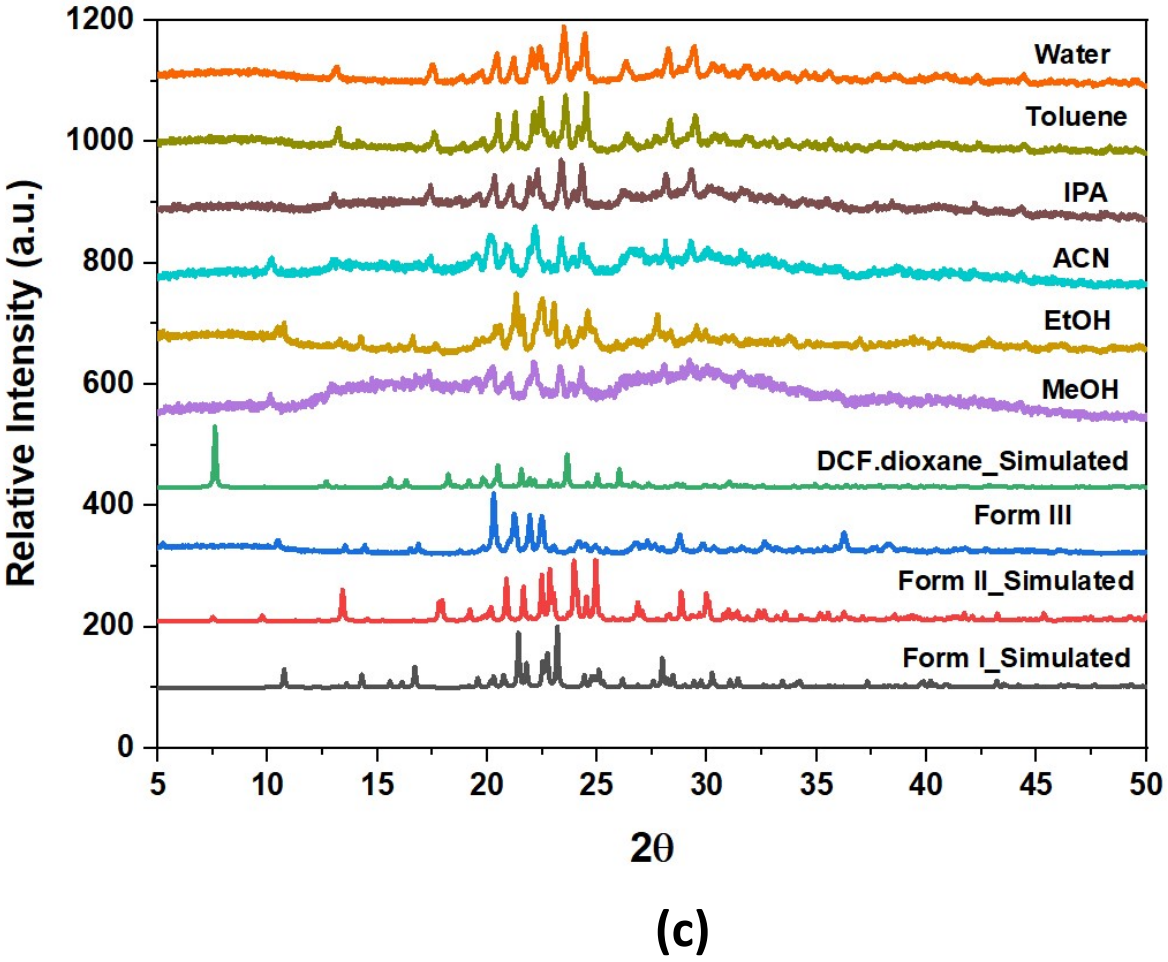
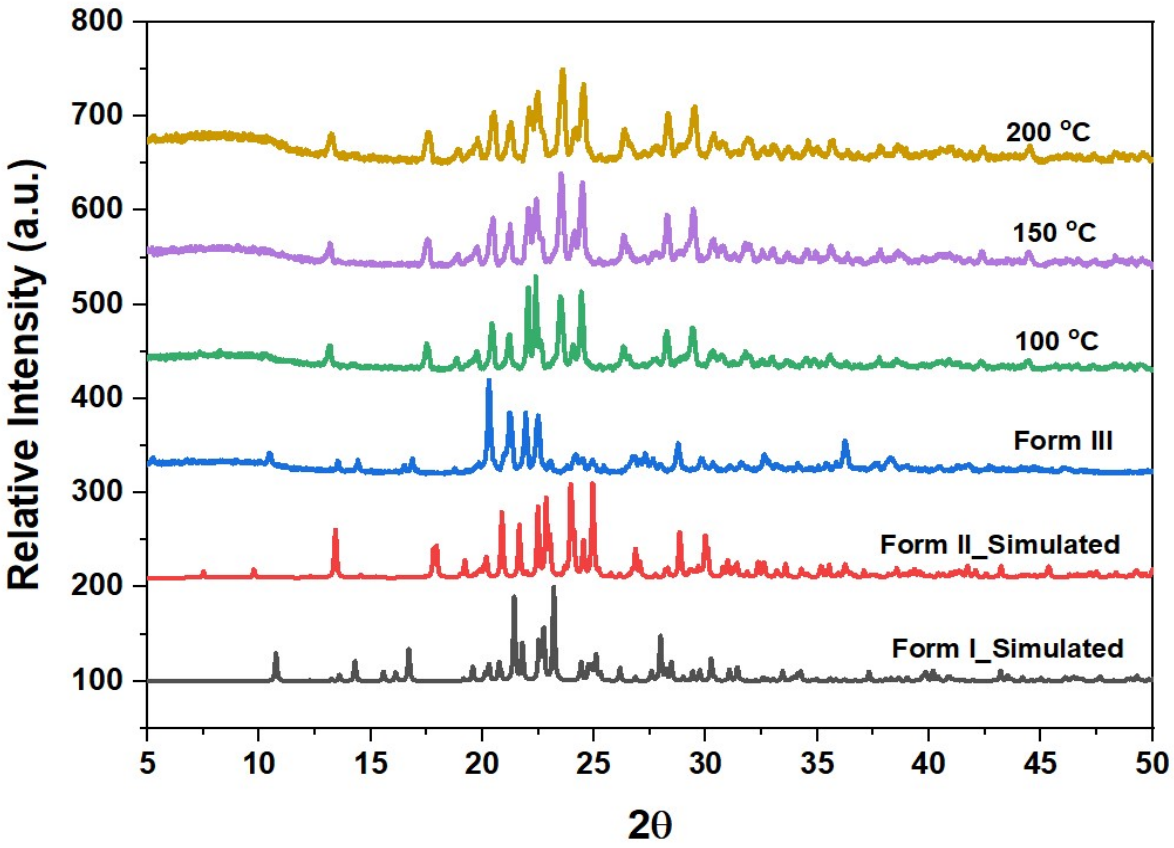
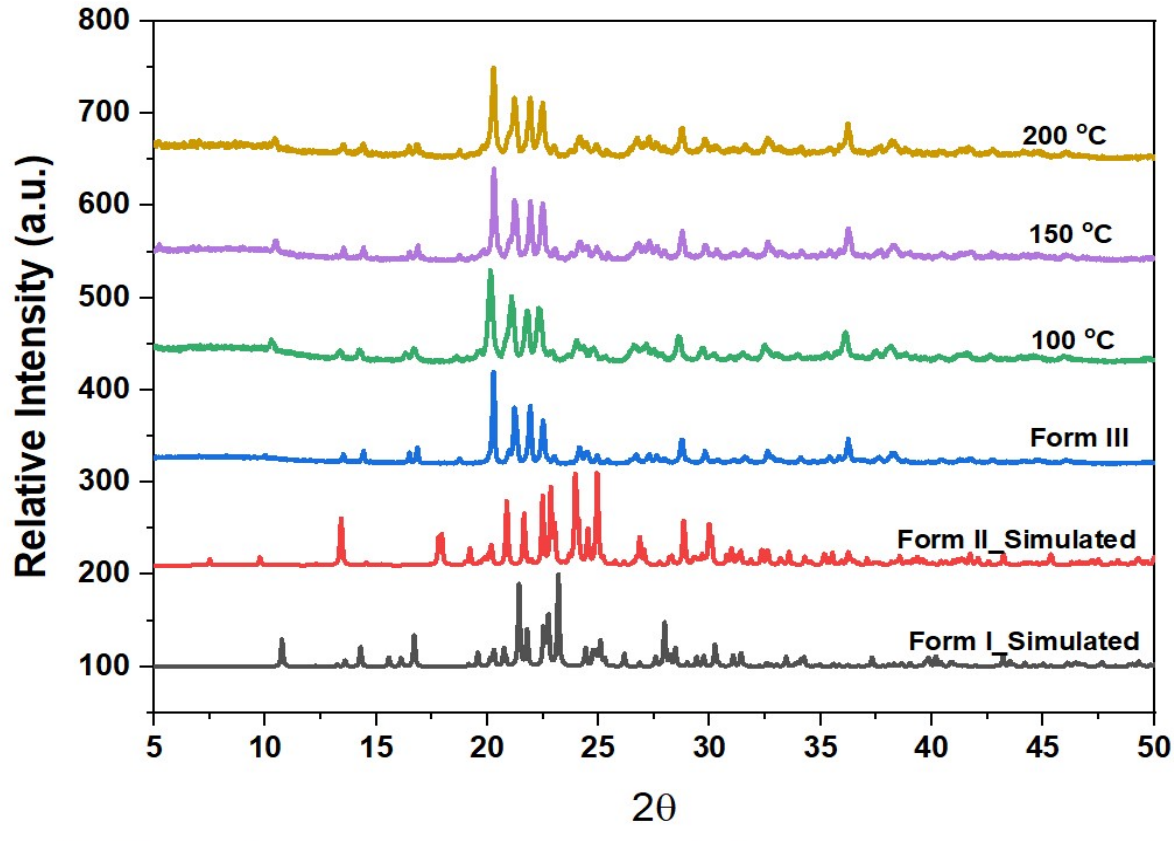


Figure S2. Stability of (a) Form II (b) Form III and (c) DCF.dioxane in different solvent media.


Relative Intensity (a.u.)
800
700
600
500
400
300
200
100
200 °C
150 °C
100 °C
Form III
Form II_Simulated
Form I_Simulated
5
10
15
20
25
30
35
40
45
50
2θ

(a)


Relative Intensity (a.u.)
800
700
600
500
400
300
200
100
200 °C
150 °C
100 °C
Form III
Form II_Simulated
Form I_Simulated
5
10
15
20
25
30
35
40
45
50
2θ

(b)

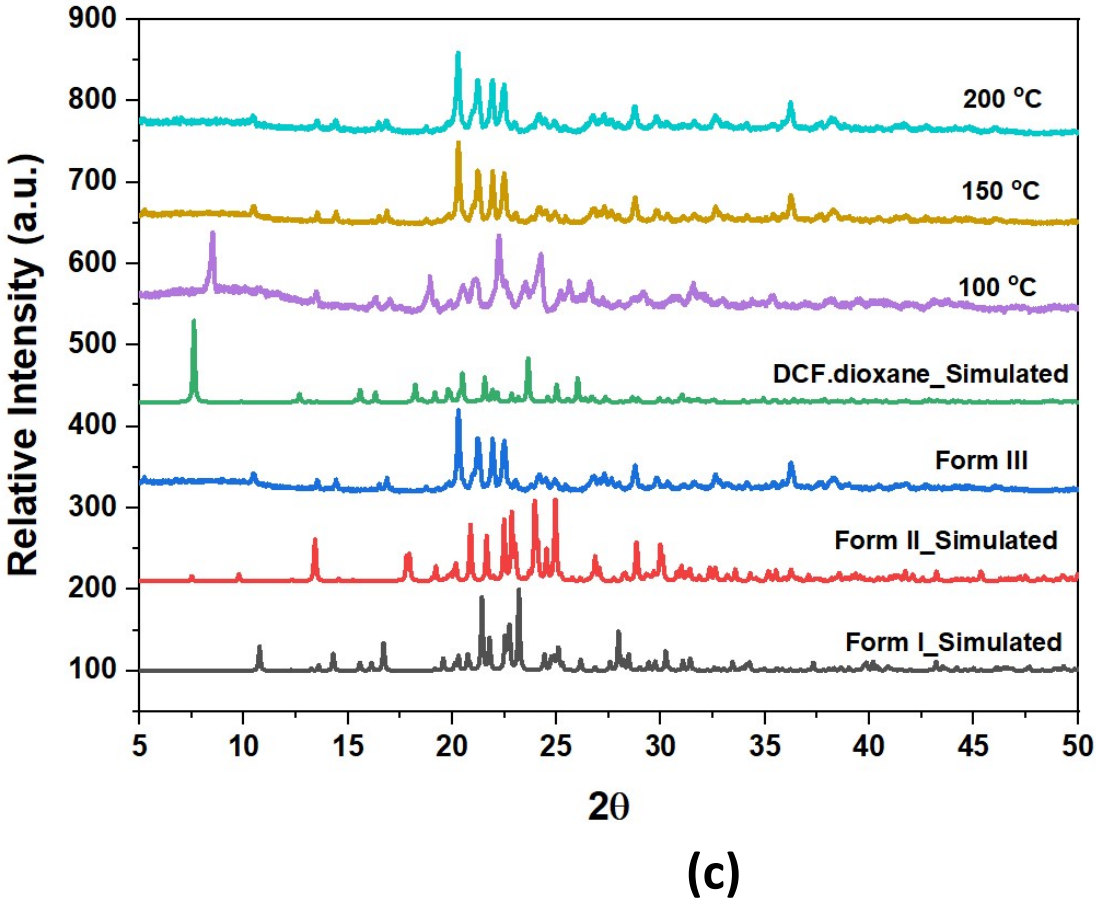
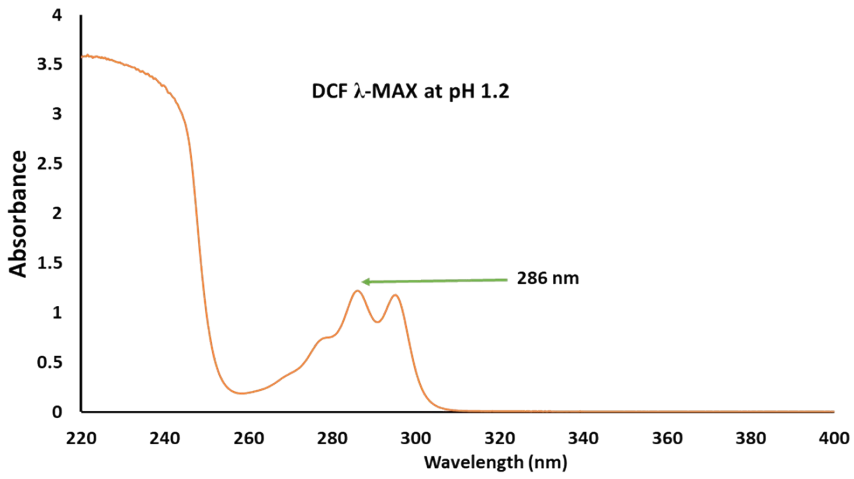
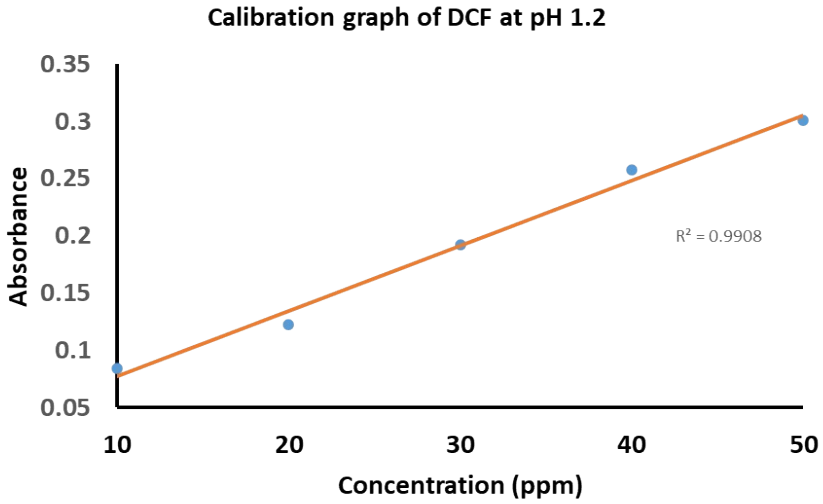
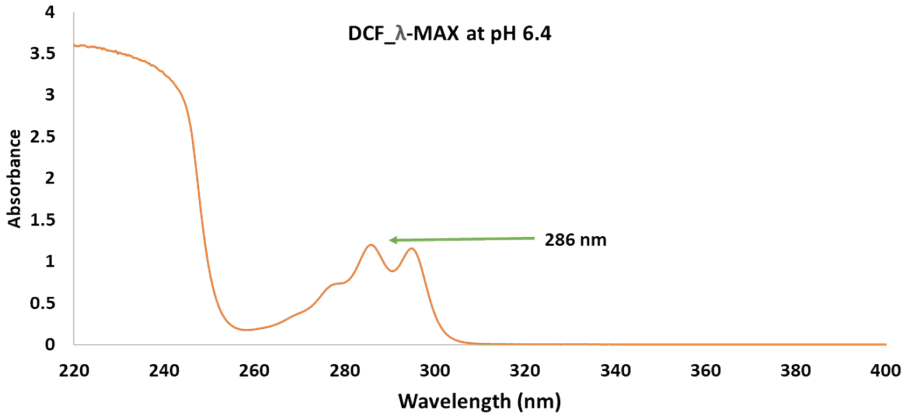


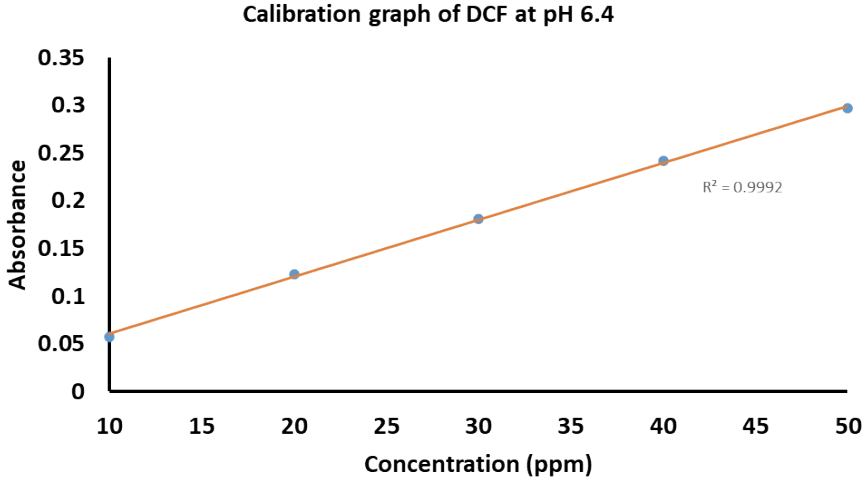
Figure S3. VT-PXRD overlay of (a) Form II (b) Form III and (c) DCF.dioxane.

Details of the solubility parameters of solid forms of DCF




Calibration graph of DCF at pH 1.2
Absorbance
0.35
0.3
0.25
0.2
0.15
0.1
0.05
R² = 0.9908
10
20
30
40
50
Concentration (ppm)


DCF_λ-MAX at pH 6.4
Absorbance
4
3.5
3
2.5
2
1.5
1
0.5
0
286 nm
220
240
260
280
300
320
340
360
380
400
Wavelength (nm)


Calibration graph of DCF at pH 6.4
Absorbance
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
R² = 0.9992
10
15
20
25
30
35
40
45
50
Concentration (ppm)