A current insight into the drug-drug molecular adducts of an anti-cancer drug Vandetanib with various NSAIDs

K G Abishek,[a] Gowtham Kenguva,[a] Lopamudra Giri,*[b] E. V. Venkat Shivaji Ramarao,[c] Gorja Dhilli Rao,[d] Rambabu Dandela*[a]

[a]Department of Industrial and Engineering Chemistry, Institute of Chemical Technology-Indian Oil Odisha Campus, Bhubaneswar, India. E-mail: r.dandela@iocb.ictmumbai.edu.in

[b]Department of Chemistry, Odisha University of Technology and Research, (Formerly CET), Bhubaneswar, India. E-mail: lopamudra7giri@gmail.com

[c]Dr Reddy's Institute of Life Sciences, University of Hyderabad Campus, Gachibowli, Hyderabad 500 046, India

[d]MLR Institute of Technology, Laxman Reddy Avenue, Dundigal, Hyderabad, Telangana 500043

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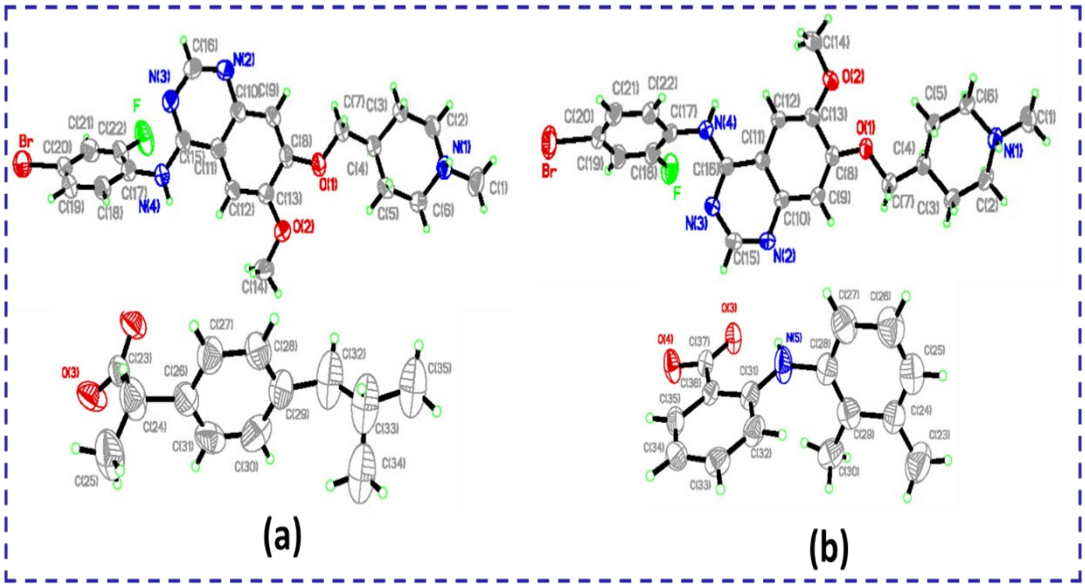

Figure S1. ORTEP view of (a) VDTB.IBU and (b) VDTB.MEF. Herein, the ellipsoids are drawn with a 50% probability.

Parameter	VDTB.IBU	VDTB.MEF
Formula	$C_{35}H_{42}BrFN_4O_4$	$C_{37}H_{39}BrFN_5O_4$
M_r	681.63	716.64
crystal shape	Block	Block
crystal colour	Colourless	Colourless
crystal system	Triclinic	Triclinic
space group	$P\bar{1}$	$P\bar{1}$
T, K	298.15	298.15
λ(Mo-K_a)/Å	0.71073	0.71073
a/Å	10.192(3)	12.7596(10)
b/Å	13.023(4)	12.7738(10)
c/Å	13.452(4)	13.1770(11)
α/^{0}	94.774(8)	110.597(2)
β/^{0}	105.146(8)	90.033(2)
γ/0	94.739(7)	118.704(2)
V/Å^3	1707.4(9)	1725.4(2)
Z	2	2
D_c / g cm^{-3}	1.326	1.379
μ, mm^{-1}	1.252	1.244
2θ range [^{0}]	2.25 - 27.59	2.23 - 27.54
limiting indices	-13 ≤ *h* ≤ 13 -16 ≤ *k* ≤ 16 -16 ≤ *l* ≤ 17	-16 ≤ *h* ≤ 16 -16 ≤ *k* ≤ 16 -17 ≤ *l* ≤ 17
F (000)	712.0	744
Total reflections	54637	33222
Unique reflections	7898	7912
Reflection at *I* > 2σ (*I*)	4753	5068
No. Of parameters	393	437
R_1 , I > 2σ (I)	0.0643	0.0643
wR_2, I > 2σ (I)	0.1809	0.1377
GoF on F^2	1.026	1.009
CCDC No.	2358466	2358467

Table S1. Crystallographic table of VDTB salts

Name of the compound	*D*–H···*A*	*D*–H(Å)	H···*A*(Å)	*D*–*A*(Å)	*D*–H···*A*(°)
VDTB.IBU	$N1^{+}$–H1···$O3^{-}$	0.980	1.661	2.635(4)	170
	N4–H4···O4	0.860	1.921	2.765(4)	165
	C12–H12···$O4^{i}$	0.930	2.401	3.273(1)	151
VDTB.MEF	$N1^{+}$–H1···$O4^{-ii}$	0.980	1.621	2.592(3)	168
	N5–H5···O3(Intra)	0.860	2.020	2.680(3)	132
	N4–H4···O3	0.860	1.993	2.932(5)	143
	C12–H12···O3	0.930	2.521	3.275(4)	138
	C1–H1C···F^{iii}	0.960	2.562	3.110(5)	122

Symmetry Codes: (i) x, y-1, z; (ii) x+1, y+1, z; (iii) -x+1, -y, -z+1.

Table 2. Hydrogen bond distances (Å) and angles (o) of the molecular complexes of VDTB.

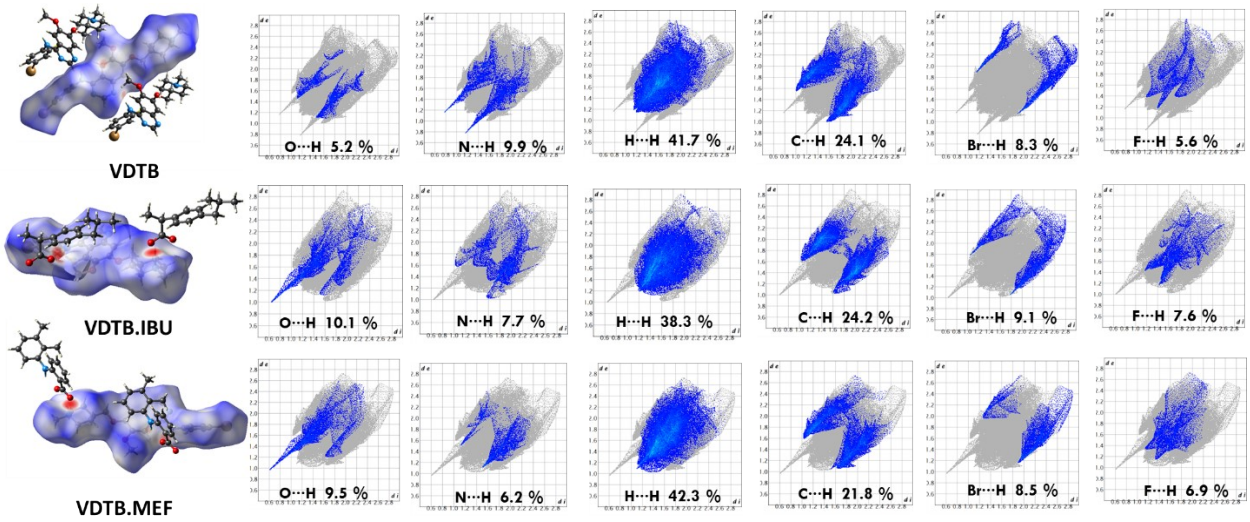

Figure S2. Hirshfield Surface analysis 3-D maps and 2-D fingerprints of VDTB and its salts VDTB.MEF and VDTB-IBU.

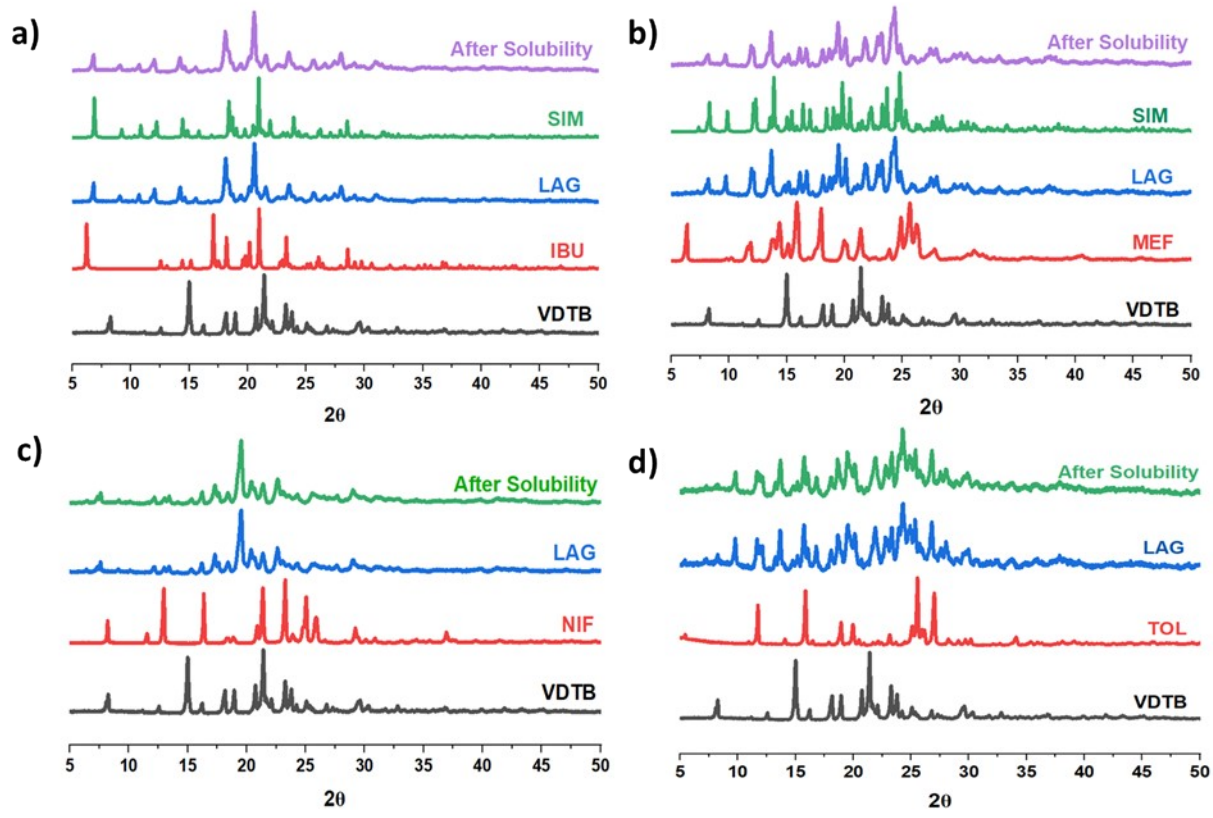

Figure S3. A comparison between the PXRD overlay of a 1:1 VDTB-NSAIDs ground combination (LAG) and its initial components.

Method development for determination of Vandetanib

For method development, the perfect quantification of VDTB was achieved using a mobile phase consisting of acetonitrile, water, and orthophosphoric acid (90:8:2 v/v/v). Such composition gave a distinct chromatographic peak with excellent resolution, a clear baseline separation, and a low tailing factor. Therefore, on this basis, this mobile phase and method of ionization were finally accepted because they gave the best peak shape, resolution and performance of the method for the quantification of VDTB. An optimum flow rate is the one that minimizes solvent consumption while allowing for a fast run time. A flow rate of 1.0 ml/min was found to be effective in this study. This ensured successful elution of the analyte with good separation and reliable performance. Lambda max was determined to be 248 nm, at a retention time (RT) of 2.94 minutes corresponding to the elution of VDTB.

Calibration curve

Concentration	Average Area under the curve
10	5.2103
20	12.7637
30	17.7232
40	23.7651
50	30.9261

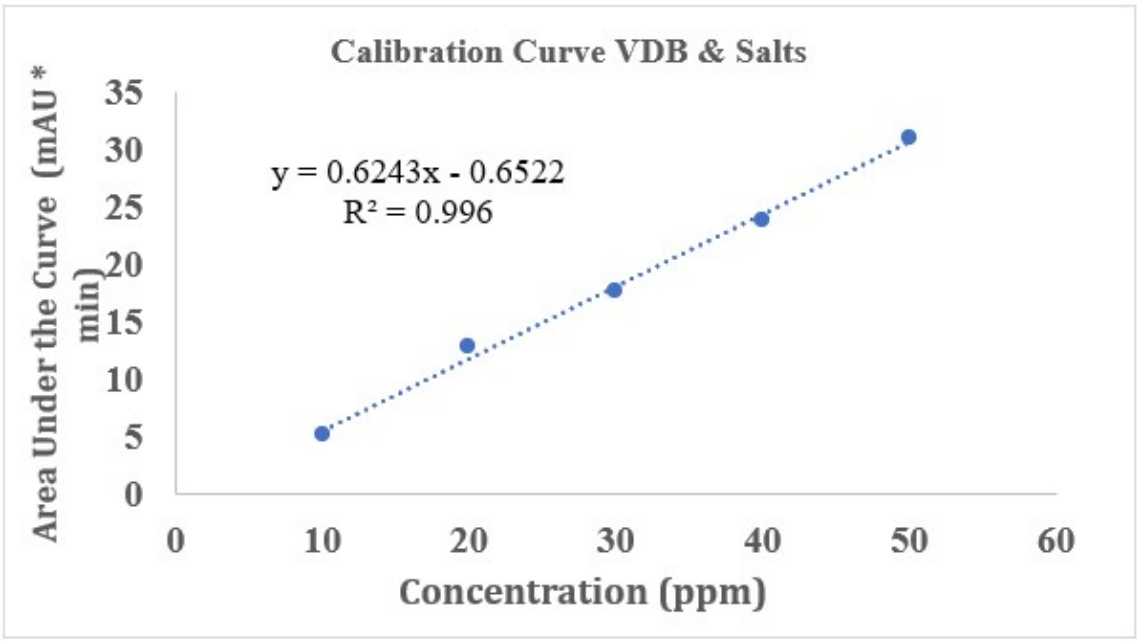

Figure S4.

Sample	First	Second	Third	Average	SD
Pure VDTB	14.36	13.96	15.06	14.46	0.56
VDTB_MEF	21.53	22.82	23.05	22.47	0.82
VDTB_NIF	37.13	36.92	41.01	38.35	2.30
VDTB_IBU	79.24	76.86	75.24	77.11	2.01
VDTB_TOL	4.92	5.37	7.44	5.91	1.34

Table S3

Time (minutes)	Pure VDTB	VDTB_MEF	VDTB_NIF	VDTB_IBU	VDTB_TOL
15	0.68	1.05	1.80	3.61	0.28
30	1.32	2.06	3.51	7.05	0.54
45	1.94	3.01	5.14	10.34	0.79
60	2.52	3.92	6.70	13.46	1.03
90	3.62	5.62	9.59	19.29	1.48
120	4.61	7.16	12.22	24.58	1.88
150	5.51	8.56	14.61	29.38	2.25
180	6.33	9.83	16.78	33.75	2.59
240	7.75	12.04	20.55	41.32	3.17
360	9.89	15.36	26.22	52.73	4.04
720	13.01	20.22	34.52	69.40	5.32

Table S4

Figure S4 and Table S3&S4. Linearity graphs for solubility and dissolution studies of VDTB salts in pH 7.0 medium.