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The influence of salt formation on electrostatic and compression properties of flurbiprofen salts

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Tables

Table 1: Parent drug and selection of counterions used in this research.

Parent drug	Acronym	Manufacturer	Chemical Formula	pKa	CLogP
Flurbiprofen	F	<i>Aesica, UK</i>	$C_{15}H_{13}FO_2$	4.4	3.44
Amines	Acronym	Manufacturer	Formula	pKa	CLogP
Butylamine	But	<i>Sigma Aldrich, USA</i>	$C_4H_9NH_2$	10.3	0.92
Octylamine	Oct	<i>Fluka, USA</i>	$C_8H_{17}NH_2$	10.3	3.04
Benzylamine	Benz	<i>Acros, USA</i>	$C_6H_5CH_2NH_2$	9.4	1.09
Cyclo-hexylamine	C-hex	<i>Lancaster, UK</i>	$C_6H_{11}NH_2$	10.5	1.98
Tert-butylamine	T-but	<i>Sigma Aldrich, USA</i>	$(CH_3)_3CNH_2$	10.5	0.59
2-amino-2-methylpropan-1-ol	AMP1	<i>Fluka, USA</i>	$C_4H_{11}NO$	9.2	-0.59
Tris(hydroxymethyl)aminomethane	Tris	<i>Sigma Aldrich, USA</i>	$(HOCH_2)_3CNH_2$	6.4	-0.94

Table 2: Classification on the basis of Heckel parameter, P_y (Nordström *et al.*, 2012).

Heckle parameter, P_y	Characteristics of compacts
< 40 Mpa	Very soft
40 Mpa < P_y < 80MPa	Soft
80 MPa < P_y < 200MPa	Moderately hard
P_y > 200 MPa	Hard

Table 3: Physicochemical and mechanical properties of flurbiprofen and its salts.

	Q_{sat} (nC/g)	Adhesion (%)	Density (g/cm ³)	M_p (°C)	Solubility (mol/L)*	d₁₀ (µm)	d₅₀ (µm)	d₉₀ (µm)	Particle Shape	b⁻¹ (MPa)	P_y (MPa)	Compact characteristics
FBP	-226	46	1.315	115	7.72x10⁻⁴	8	20	43	Equant	7.9 (1.4)	70.2 (2.6)	Soft
F-But	-17	12	1.199	146	0.0489	8	40	190	Prism	7.5 (1.2)	84.1 (1.9)	Moderately hard
F-Oct	-18	15	1.129	102	3.69x10 ⁻³	11	28	61	Tabular	8.2 (0.8)	110.6 (2.3)	Moderately hard
F-Benz	-75	16	1.237	136	8.01x10 ⁻³	24	128	265	Needle	8.1 (0.9)	91.2 (1.0)	Moderately hard
F-Chex	+31	12	1.229	209	0.0126	9	57	132	Needle	8.3 (0.5)	114.4 (1.4)	Moderately hard
F-Tbut	+7	6	1.240	184	0.0435	9	65	149	Needle	7.4 (0.5)	62.91 (1.4)	Soft
F-AMP1	-350	32	1.319	154	0.199	8	95	194	Needle	13.0 (0.1)	228.0 (1.2)	Hard
F-Tris	-70	25	1.424	152	0.248	13	102	189	Columnar	13.5 (0.7)	242.0 (2.8)	Hard

Q_{sat} Electrostatic charge at saturation point

M_p Melting point

P_y Mean yield pressure (Heckel parameter)

b⁻¹

*

Pressure required to reduce the powder bed to 50% (Kawakita parameter)

Aqueous solubility data (David *et al.*, 2012)

Table 4: Unit cell dimensions, intermolecular distances and intermolecular angles for F-Tbut, F-AMP1 and F-Tris salts (Schwalbe *et al.*, 2010).

Parameter	F-Tbut	F-AMP1	F-Tris
$a / \text{\AA}$	15.9343	16.1330	6.1930
$b / \text{\AA}$	6.2903	6.2700	9.9421
$c / \text{\AA}$	19.1949	18.8520	14.6846
$\alpha \text{ deg}$	90.0	90.0	93.94
$\beta \text{ deg}$	114.7	114.7	90.03
$\gamma \text{ deg}$	90.0	90.0	90.72

Intermolecular distances / \AA

O1 – H1B	1.869	1.880	3.158
O1 – H1A	1.863	1.856	1.924
O1 – H4	7.107	7.007	1.795
O2 – H1C	1.882	1.888	1.922
O1 – N1	2.767	2.760	2.771
O2 – N1	2.790	2.797	2.809
O2 – O3	-	4.002	2.692
O3 – H3F	-	2.022	3.480
F1 – F2	2.515	2.587	6.307
F1 – H8	2.675	2.688	3.166
F1 – H18	2.940	2.820	2.761
F2 – H11	2.445	2.398	2.463

Intermolecular angles / deg

N1 – O1 - C	127.993	130.988	31.261
O2 – O1 – N1	108.024	111.195	48.167