

# Study of Interaction Energies between PAMAM Dendrimer and non-Steroidal Anti-Inflammatory

## Drug Using a Distributed Computational Strategy and Experimental Analysis by ESI-MS/MS.

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### SUPPLEMENTARY TABLES

**Table S1.** Energy information obtained for the complexes formed by the fragment  $n_1$  of PAMAM dendrimer and 4 NSAIDs.

drug	complex (drug + fragment)				drug $\Delta H_f$ drug kcal/mol	fragment $n_1$ $\Delta H_f$ fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	$\Delta H_f$ complex kcal/mol	$\Delta H_f^a$ final kcal/mol				
Naproxen	-15,52	-4,45	47,58	27,61	-39,75	242,78	-175,41	0
Ketoprofen	-15,36	-5,42	71,60	50,82	-21,30	242,78	-170,65	1,1
Ibuprofen	-14,90	-5,05	53,53	33,58	-42,19	242,78	-167,00	2,1
Diflunisal	-14,26	-6,70	-23,48	-44,43	-126,42	242,78	-160,78	2,5

**Table S2.** Energy information obtained for the complexes formed by the fragment  $n_2$  of PAMAM dendrimer and 4 NSAIDs.

drug	complex (drug + fragment)				drug $\Delta H_f$ drug kcal/mol	fragment $n_2$ $\Delta H_f$ fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	$\Delta H_f$ complex kcal/mol	$\Delta H_f^a$ final kcal/mol				
Naproxen	-13,01	-3,19	-54,75	-70,95	-21,30	120,53	-170,18	0
Ketoprofen	-11,50	-3,66	-69,72	-84,88	-39,75	120,53	-165,66	1,1
Ibuprofen	-11,16	-3,52	-71,25	-85,93	-42,19	120,53	-164,27	2,1
Diflunisal	-10,15	-6,17	-153,64	-169,96	-126,42	120,53	-164,07	2,5

**Table S3.** Energy information obtained for the complexes formed by the fragment  $n_3$  of PAMAM dendrimer and 4 NSAIDs.

drug	complex (drug + fragment)				drug $\Delta H_f$ drug kcal/mol	fragment $n_3$ $\Delta H_f$ fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	$\Delta H_f$ complex kcal/mol	$\Delta H_f^a$ final kcal/mol				
Naproxen	-13,89	-3,57	183,34	165,88	-21,30	296,41	-109,22	0
Ketoprofen	-13,78	-5,59	177,56	158,19	-42,19	296,41	-96,03	1,1
Ibuprofen	-13,78	-6,70	97,69	77,21	-126,42	296,41	-92,77	2,1
Diflunisal	-13,30	-3,91	182,46	165,25	-39,75	296,41	-91,41	2,5

**Table S4.** Energy information obtained for the complexes formed by the fragment  $n_4$  of PAMAM dendrimer and 4 NSAIDs.

drug	complex (drug + fragment)				drug $\Delta H_f$ drug kcal/mol	fragment $n_4$ $\Delta H_f$ fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	$\Delta H_f$ complex kcal/mol	$\Delta H_f^a$ final kcal/mol				
Naproxen	-15,52	-4,45	47,58	27,61	-39,75	242,78	-175,41	0
Ketoprofen	-15,36	-5,42	71,60	50,82	-21,30	242,78	-170,65	1,1
Ibuprofen	-14,90	-5,05	53,53	33,58	-42,19	242,78	-167,00	2,1
Diflunisal	-14,26	-6,70	-23,48	-44,43	-126,42	242,78	-160,78	2,5

**Table S5. Energy information obtained for the complexes formed by the fragment n<sub>5</sub> of PAMAM dendrimer and 4 NSAIDs.**

drug	complex (drug + fragment)				drug ΔHf drug kcal/mol	fragment n <sub>5</sub> ΔHf fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	ΔHf complex kcal/mol	ΔHf <sup>a</sup> final kcal/mol				
Naproxen	-39,71	-4,95	61,33	16,66	-42,19	270,59	-211,74	0
Ketoprofen	-38,97	-5,46	85,19	40,76	-21,30	270,59	-208,53	1,1
Ibuprofen	-36,42	-7,74	-2,46	-46,62	-126,42	270,59	-190,79	2,1
Diflunisal	-36,29	-4,73	85,30	44,28	-39,75	270,59	-186,57	2,5

**Table S6. Energy information obtained for the complexes formed by the fragment n<sub>6</sub> of PAMAM dendrimer and 4 NSAIDs.**

drug	complex (drug + fragment)				drug ΔHf drug kcal/mol	fragment n <sub>6</sub> ΔHf fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	ΔHf complex kcal/mol	ΔHf <sup>a</sup> final kcal/mol				
Naproxen	-37,01	-4,96	470,63	428,66	-39,75	725,78	-257,37	0
Ketoprofen	-35,99	-4,16	512,84	472,69	-21,30	725,78	-231,79	1,1
Ibuprofen	-35,85	-7,81	502,00	458,33	-42,19	725,78	-225,26	2,1
Diflunisal	-35,13	-4,18	417,54	378,24	-126,42	725,78	-221,12	2,5

**Table S7. Energy information obtained for the complexes formed by the fragment n<sub>7</sub> of PAMAM dendrimer and 4 NSAIDs.**

drug	complex (drug + fragment)				drug ΔHf drug kcal/mol	fragment n <sub>7</sub> ΔHf fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	ΔHf complex kcal/mol	ΔHf <sup>a</sup> final kcal/mol				
Naproxen	-48,80	-9,31	312,96	254,85	-39,75	486,57	-191,97	0
Ketoprofen	-47,20	-7,47	330,56	275,88	-21,30	486,57	-189,38	1,1
Ibuprofen	-46,99	-8,86	311,70	255,86	-42,19	486,57	-188,52	2,1
Diflunisal	-46,24	-7,37	227,95	174,34	-126,42	486,57	-185,80	2,5

**Table S8. Energy information obtained for the complexes formed by the fragment n<sub>8</sub> of PAMAM dendrimer and 4 NSAIDs.**

drug	complex (drug + fragment)				drug ΔHf drug kcal/mol	fragment n <sub>8</sub> ΔHf fragment kcal/mol	interaction energy <sup>b</sup>	experimental values
	dispersion contribution kcal/mol	h-bond contribution kcal/mol	ΔHf complex kcal/mol	ΔHf <sup>a</sup> final kcal/mol				
Naproxen	-59,59	-13,66	320,29	247,04	-39,75	644,24	-357,45	0
Ketoprofen	-58,72	-10,78	338,28	268,78	-21,30	644,24	-354,17	1,1
Ibuprofen	-58,12	-9,90	321,40	253,38	-42,19	644,24	-348,68	2,1
Diflunisal	-57,35	-10,56	242,95	175,04	-126,42	644,24	-342,78	2,5

<sup>a</sup> Final heat of formation is formed by the heat of formation for the complex (ΔHf<sub>complex</sub>) plus the contributions of dispersion and H-bond.

<sup>b</sup> Interaction energy is calculated as :  $\Delta Hf_{\text{complex}} - (\Delta Hf_{\text{fragment}} + \Delta Hf_{\text{drug}})$