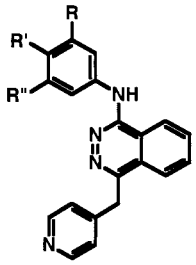
2000, Volume 43

Guido Bold,* Karl-Heinz Altmann, Jörg Frei, Marc Lang, Paul W. Manley, Peter Traxler, Bernhard Wietfeld, Josef Brüggen, Elisabeth Buchdunger, Robert Cozens, Stefano Ferrari, Pascal Furet, Francesco Hofmann, Georg Martiny-Baron, Jürgen Mestan, Johannes Rösel, Matthew Sills, David Stover, Figan Acemoglu, Eugen Boss, René Emmenegger, Laurent Lässer, Elvira Masso, Rosemari Roth, Christian Schlachter, Werner Vetterli, Dominique Wyss, and Jeanette M. Wood: New Anilinophthalazines as Potent and Orally Well Absorbed Inhibitors of the VEGF Receptor Tyrosine Kinases Useful as Antagonists of Tumor-Driven Angiogenesis.

Page 2316. In Table 3, the unit for c_{max} is wrong. The concentration should be given as [μM]. The correct version of Table 3 is as follows:

Table 3. Enzyme Inhibition of the 1-Anilino-(4-pyridylmethyl)phthalazine Derivatives **CGP 79787D**, **55**−**66**, and **SU 5416**[a]



cpd	R	R'	R''	enzymatic inhibition IC_{50} [μM] Flt-1	KDR	PDGF[b]	c-Kit	cellular[c] ED_{50} [nM] KDR	pharmacokin. c_{max}[d] [μM]	t_{max} [min]
CGP 79787D	H	Cl	H	0.077	0.037	0.6	0.7	34	32	15
55[e]	H	H	H	0.06	0.95	2.8	>10	200		
56	Me	H	H	0.04	0.08	1	2.5	8	13	30
57[e]	H	^{t}Bu	H	0.24	0.21	2	1	9	25.6	30
58	H	Ph	H	0.23	0.20	1.4	1.4	85		
59	OMe	H	H	0.33	0.24	0.8	3	37	21	30
60	OH	H	H	0.08	0.67	4	7.9	250	0.5[f]	30
61	Cl	Cl	H	0.07	0.03	0.6	0.7	27	9.8	30
62	OMe	Cl	H	0.26	0.14	2	3.5	24	8.0	30
63	Me	H	Me	0.15	0.04	0. 8	2.0	10	10.0	30
64	CF_3	Cl	H	0.6	0.3	4	2.7	27	7.6	120
65	CF_3	H	Br	0.6	0.38	>10	>10	39	6.0	120
66	CF_3	H	F	0.35	0.20	>10	>10	40		
SU 5416				0.008	0.20	0.68	0.4	930	0.3	30

[a] The data represent averages of at least three determinations. [b] PDGF-β receptor. [c] Inhibition of VEGF-driven cellular receptor autophosphorylation in CHO cells transfected with the KDR receptor. [d] The pharmacokinetic studies were performed in mice: Drug concentrations in blood samples were analyzed by reversed-phase HPLC 30, 60, 90, and 120 min after oral application of 50 mg/kg in a standardized formulation (DMSO/Tween 80). The value c_{max} represents the highest observed drug concentration at the indicated time point (t_{max}). [e] Dihydrochloride salt. [f] Low concentration of the parent compound but an apparently high concentration (not determined) of an unknown metabolite.

JM001010D

10.1021/jm001010d
Published on Web 07/27/2000