

(Toets Bereiding en Analyse (Fa-202))
1 november 2013, 13.30-16.30 uur
Educatorium Alfa

Vermeld duidelijk uw naam en studentnummer op elk vel. Gebruik de kaders om te schrijven. Maak de vellen niet los.

Controleer of het tentamen compleet is (8 vragen, 22 blz. Bijlage met 8 bladzijden).

Geef duidelijk maar bondig antwoord op de gestelde vragen. Bij de beoordeling en becijfering wordt gelet op volledigheid van het antwoord, op de afwezigheid van overbodige en niet ter zake doende informatie, en op de juistheid en precisie van de formulering van het antwoord.

Beargumenteer uw antwoord altijd.

Laat berekeningen stapsgewijs zien en let op het aantal significante cijfers in het eindantwoord. De vragen 2c, 2d, 4c, 5d en 8c worden ook beoordeeld voor het portfolio rekenvaardigheid.

Voor dit tentamen kunnen in totaal 100 punten worden behaald. De uitslag wordt bekend gemaakt via blackboard

HIERACHTER VIND U DE BIJLAGEN

Enkele formules:

$$C_t = C_0 \cdot e^{-kt}$$

$$dm/dt = DA(C_s - C)/h$$

$$V_s = V_{SL} + V_L \cos\theta$$

$$\ln S/S_0 = 2\gamma M / rdRT$$

$$pH = pK_a + \log [A^-]/[HA]$$

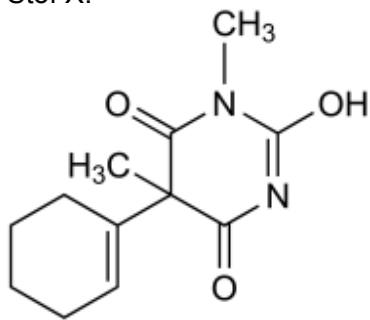
$$\beta = 2.3 \cdot C \cdot K_a \cdot [H^+] / (K_a + [H^+])^2$$

$$\text{Inhoud bol: } 4/3r^3$$

$$\text{oppervlakte cirkel: } 2\pi r^2$$

Informatie bij vraag 2

Stof X:



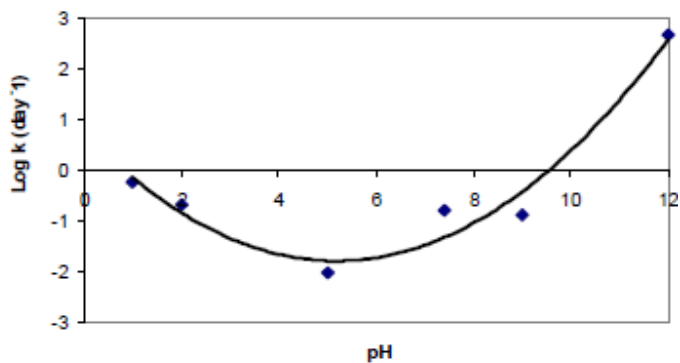
$C_{12}H_{16}N_2O_3 = 236.3$

Colourless crystals or a white crystalline powder. M.p. 145° to 147°.

Practically insoluble in water; soluble 1 in 45 of ethanol, 1 in 4 of chloroform, and 1 in 80 of ether; soluble in acetone, benzene, and methanol.

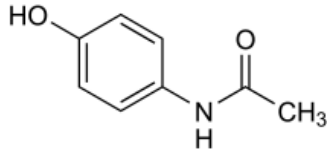
pKa: 8.2 (20°).

Resultaat van een ontledingsonderzoek: pH-ontledingsprofiel (20°C), stof X gepreformuleerd bij verschillende pH's:



Informatie bij vraag 5 en 7

Paracetamol (uit Clarke's)

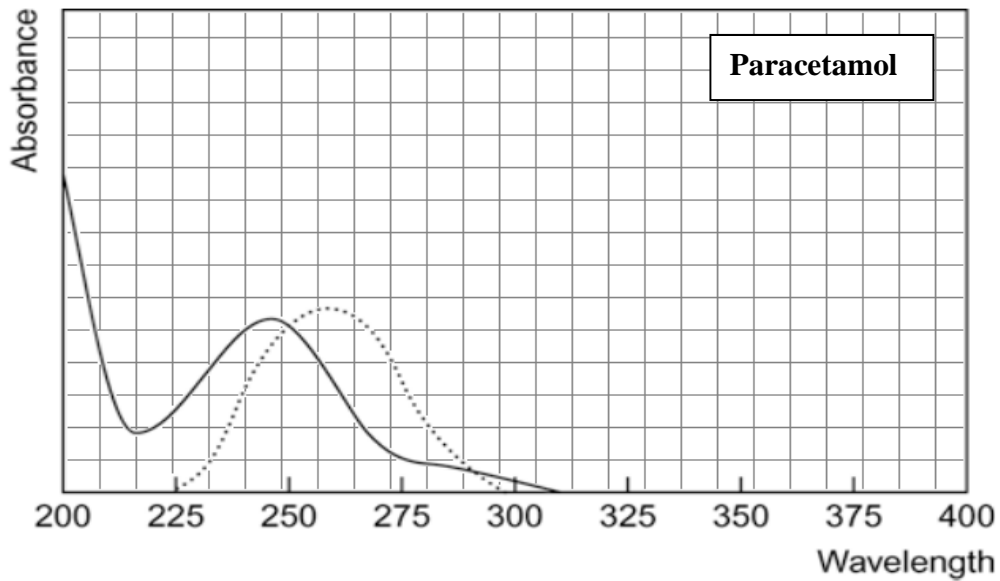


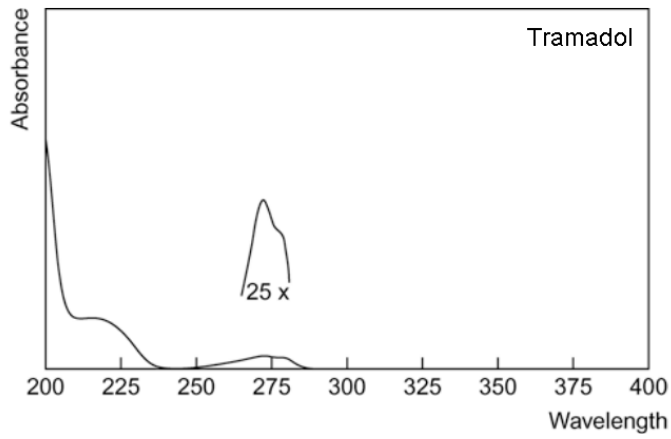
Very slightly soluble in cold water, considerably more soluble in hot water; soluble in ethanol, methanol, dimethylformamide, ethylene dichloride, acetone, and ethyl acetate; very slightly soluble in chloroform; slightly soluble in ether; practically insoluble in petroleum ether, pentane, and benzene.

Dissociation Constant. pK_a 9.5 (25°).

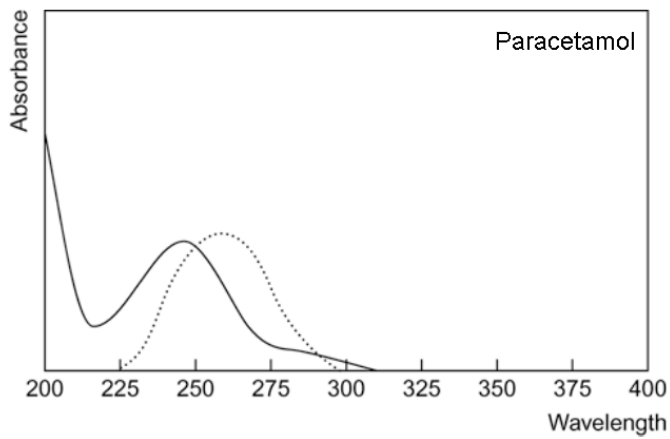
Partition Coefficient. Log P (octanol/water), 0.5.

Ultraviolet Spectrum. Aqueous acid—245 ($A^1_1=668a$); aqueous alkali—257 nm ($A^1_1=715a$).





Tramadol: Aqueous acid—272 ($A_1 = 70$),
shoulder at 279 nm. No alkaline shift.



Paracetamol: Aqueous acid—245 nm ($A_1 = 668a$); aqueous alkali—257 nm ($A_1 = 715a$)

Samenvatting EP 2.9.40

Eis: $AV \leq 15$

$$AV = |M - \bar{X}| + k \cdot s$$

If 98.5 per cent $\leq \bar{X} \leq$ 101.5 per cent, then	$M = \bar{X}$ ($AV = ks$)
If $\bar{X} < 98.5$ per cent, then	$M = 98.5$ per cent ($AV = 98.5 - \bar{X} + ks$)
If $\bar{X} > 101.5$ per cent, then	$M = 101.5$ per cent ($AV = \bar{X} - 101.5 + ks$)

n	k
5	3.2
6	3.0
7	2.8
8	2.6
10	2.4
30	2.0

Table 2.9.40.-1 – Application of Content Uniformity (CU) and Mass Variation (MV) test for dosage forms

Dosage forms	Type	Sub-Type	Dose and ratio of active substance	
			≥ 25 mg and ≥ 25 per cent	< 25 mg or < 25 per cent
Tablets	uncoated		MV	CU
	coated	film-coated	MV	CU
		others	CU	CU
Capsules	hard		MV	CU
	soft	suspensions, emulsions, gels	CU	CU
		solutions	MV	MV
Solids in single-dose containers	single component		MV	MV
	multiple components	solution in freeze-dried final container	MV	MV
		others	CU	CU
Solutions enclosed in single-dose containers			MV	MV
Others			CU	CU

Informatie bij vraag 8:

Bijlage: Statistiekformules en tabellen

$$\sigma_y = \sqrt{\sigma_a^2 + \sigma_b^2} \quad RSD_y = \sqrt{RSD_a^2 + RSD_b^2} \quad RSD = \frac{\sigma_y}{y} * 100\%$$

$$RSD_y = \sqrt{RSD_a^2 + RSD_b^2 + RSD_c^2 + RSD_d^2 + RSD_e^2} \quad F = \frac{s_{grootste}^2}{s_{kleinste}^2}$$

$$Q = \frac{\text{maximum} - \text{naastliggende}}{\text{range}} \text{ of } Q = \frac{\text{naastliggende} - \text{minimum}}{\text{range}}$$

$$r = \frac{\sum_{i=1}^n (X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum_{i=1}^n (X_i - \bar{X})^2 \sum_{i=1}^n (Y_i - \bar{Y})^2}} \quad T = \frac{r}{\sqrt{(1-r^2)/(n-2)}} \sim t_{n-2}$$

$$b = \frac{\sum_{i=1}^n (X_i - \bar{X})(Y_i - \bar{Y})}{\sum_{i=1}^n (X_i - \bar{X})^2} \quad a = \bar{Y} - b * \bar{X} \quad T = \frac{b}{SE(b)} \sim t_{n-2}$$

$$SE(b) = \sqrt{\frac{s^2}{\sum (X - \bar{X})^2}} \quad SE(a) = \sqrt{\frac{s^2 \sum X_i^2}{n \sum (X - \bar{X})^2}}$$

$$s = \sqrt{\frac{\sum_{i=1}^n (Y_i - (a + bX_i))^2}{(n-2)}}$$

$$SE(\hat{Y}_0) = s * \sqrt{\frac{1}{m} + \frac{1}{n} + \frac{(X_0 - \bar{X})^2}{\sum (X - \bar{X})^2}}$$

$$SE(\hat{X}_0) = \sqrt{\frac{s^2}{b^2} \left(\frac{1}{m} + \frac{1}{n} + \frac{(Y_0 - \bar{Y})^2}{b^2 \sum (X - \bar{X})^2} \right)}$$

n	Q _{.10}	Q _{.05}
3	0.941	0.970
4	0.765	0.829
5	0.642	0.710
6	0.560	0.625
7	0.507	0.568
8	0.448	0.526
9	0.437	0.493
10	0.412	0.466

Tabel A1 Standard Normal distribution
Tabel A2 t-distribution
Tabel A4 F-distribution

Tabel A1	
Z	Two-tailed P-value
0.0	1.000
0.1	0.920
0.2	0.841
0.3	0.764
0.4	0.689
0.5	0.617
0.6	0.549
0.7	0.484
0.8	0.424
0.9	0.368
1.0	0.317
1.1	0.271
1.2	0.230
1.3	0.194
1.4	0.162
1.5	0.134
1.6	0.110
1.7	0.089
1.8	0.072
1.9	0.057
2.0	0.046
2.1	0.036
2.2	0.028
2.3	0.021
2.4	0.016
2.5	0.012
2.6	0.009
2.7	0.007
2.8	0.005
2.9	0.004
3.0	0.003
3.1	0.002
3.2	0.001
3.3	0.001
3.4	0.001
3.5	0.000

Tabel A2				
df	Two-tailed P-value			
	0.1	0.05	0.01	0.001
1	6.314	12.706	63.657	636.619
2	2.920	4.303	9.925	31.599
3	2.353	3.182	5.841	12.924
4	2.132	2.776	4.604	8.610
5	2.015	2.571	4.032	6.869
6	1.943	2.447	3.707	5.959
7	1.895	2.365	3.499	5.408
8	1.860	2.306	3.355	5.041
9	1.833	2.262	3.250	4.781
10	1.812	2.228	3.169	4.587
11	1.796	2.201	3.106	4.437
12	1.782	2.179	3.055	4.318
13	1.771	2.160	3.012	4.221
14	1.761	2.145	2.977	4.140
15	1.753	2.131	2.947	4.073
16	1.746	2.120	2.921	4.015
17	1.740	2.110	2.898	3.965
18	1.734	2.101	2.878	3.922
19	1.729	2.093	2.861	3.883
20	1.725	2.086	2.845	3.850
21	1.721	2.080	2.831	3.819
22	1.717	2.074	2.819	3.792
23	1.714	2.069	2.807	3.768
24	1.711	2.064	2.797	3.745
25	1.708	2.060	2.787	3.725
26	1.706	2.056	2.779	3.707
27	1.703	2.052	2.771	3.690
28	1.701	2.048	2.763	3.674
29	1.699	2.045	2.756	3.659
30	1.697	2.042	2.750	3.646
40	1.684	2.021	2.704	3.551
50	1.676	2.009	2.678	3.496
100	1.660	1.984	2.626	3.390
200	1.653	1.972	2.601	3.340
5000	1.645	1.960	2.577	3.292

Table A4		df of numerator													
df of denominator	2-tailed P-value	1-tailed P-value	1	2	3	4	5	6	7	8	9	10	15	25	500
1	0.05	0.025	647.79	799.50	864.16	899.58	921.85	937.11	948.22	956.66	963.28	968.63	984.87	998.08	1017.24
1	0.1	0.05	161.45	199.50	215.71	224.58	230.16	233.99	236.77	238.88	240.54	241.88	245.95	249.26	254.06
2	0.05	0.025	38.51	39.00	39.17	39.25	39.30	39.33	39.36	39.37	39.39	39.40	39.43	39.46	39.50
2	0.1	0.05	18.51	19.00	19.16	19.25	19.30	19.33	19.35	19.37	19.38	19.40	19.43	19.46	19.49
3	0.05	0.025	17.44	16.04	15.44	15.10	14.88	14.73	14.62	14.54	14.47	14.42	14.25	14.12	13.91
3	0.1	0.05	10.13	9.55	9.28	9.12	9.01	8.94	8.89	8.85	8.81	8.79	8.70	8.63	8.53
4	0.05	0.025	12.22	10.65	9.98	9.60	9.36	9.20	9.07	8.98	8.90	8.84	8.66	8.50	8.27
4	0.1	0.05	7.71	6.94	6.59	6.39	6.26	6.16	6.09	6.04	6.00	5.96	5.86	5.77	5.64
5	0.05	0.025	10.01	8.43	7.76	7.39	7.15	6.98	6.85	6.76	6.68	6.62	6.43	6.27	6.03
5	0.1	0.05	6.61	5.79	5.41	5.19	5.05	4.95	4.88	4.82	4.77	4.74	4.62	4.52	4.37
6	0.05	0.025	8.81	7.26	6.60	6.23	5.99	5.82	5.70	5.60	5.52	5.46	5.27	5.11	4.86
6	0.1	0.05	5.99	5.14	4.76	4.53	4.39	4.28	4.21	4.15	4.10	4.06	3.94	3.83	3.68
7	0.05	0.025	8.07	6.54	5.89	5.52	5.29	5.12	4.99	4.90	4.82	4.76	4.57	4.40	4.16
7	0.1	0.05	5.59	4.74	4.35	4.12	3.97	3.87	3.79	3.73	3.68	3.64	3.51	3.40	3.24
8	0.05	0.025	7.57	6.06	5.42	5.05	4.82	4.65	4.53	4.43	4.36	4.30	4.10	3.94	3.68
8	0.1	0.05	5.32	4.46	4.07	3.84	3.69	3.58	3.50	3.44	3.39	3.35	3.22	3.11	2.94
9	0.05	0.025	7.21	5.71	5.08	4.72	4.48	4.32	4.20	4.10	4.03	3.96	3.77	3.60	3.35
9	0.1	0.05	5.12	4.26	3.86	3.63	3.48	3.37	3.29	3.23	3.18	3.14	3.01	2.89	2.72
10	0.05	0.025	6.94	5.46	4.83	4.47	4.24	4.07	3.95	3.85	3.78	3.72	3.52	3.35	3.09
10	0.1	0.05	4.96	4.10	3.71	3.48	3.33	3.22	3.14	3.07	3.02	2.98	2.85	2.73	2.55
15	0.05	0.025	6.20	4.77	4.15	3.80	3.58	3.41	3.29	3.20	3.12	3.06	2.86	2.69	2.41
15	0.1	0.05	4.54	3.68	3.29	3.06	2.90	2.79	2.71	2.64	2.59	2.54	2.40	2.28	2.08
20	0.05	0.025	5.87	4.46	3.86	3.51	3.29	3.13	3.01	2.91	2.84	2.77	2.57	2.40	2.10
20	0.1	0.05	4.35	3.49	3.10	2.87	2.71	2.60	2.51	2.45	2.39	2.35	2.20	2.07	1.86
30	0.05	0.025	5.57	4.18	3.59	3.25	3.03	2.87	2.75	2.65	2.57	2.51	2.31	2.12	1.81
30	0.1	0.05	4.17	3.32	2.92	2.69	2.53	2.42	2.33	2.27	2.21	2.16	2.01	1.88	1.64
50	0.05	0.025	5.34	3.97	3.39	3.05	2.83	2.67	2.55	2.46	2.38	2.32	2.11	1.92	1.57
50	0.1	0.05	4.03	3.18	2.79	2.56	2.40	2.29	2.20	2.13	2.07	2.03	1.87	1.73	1.46
100	0.05	0.025	5.18	3.83	3.25	2.92	2.70	2.54	2.42	2.32	2.24	2.18	1.97	1.77	1.38
100	0.1	0.05	3.94	3.09	2.70	2.46	2.31	2.19	2.10	2.03	1.97	1.93	1.77	1.62	1.31
1000	0.05	0.025	5.04	3.70	3.13	2.80	2.58	2.42	2.30	2.20	2.13	2.06	1.85	1.64	1.16
1000	0.1	0.05	3.85	3.00	2.61	2.38	2.22	2.11	2.02	1.95	1.89	1.84	1.68	1.52	1.13