BAB 5
SIMPULAN

5.1 Simpulan

1. Senyawa *O*-(asetil)parasetamol dapat disintesis melalui reaksi asilasi antara parasetamol dan asetil klorida.
2. Senyawa *O*-(asetil)parasetamol mempunyai aktivitas analgesik yang tidak berbeda bermakna dibanding parasetamol pada dosis 25, 50 dan 100 mg/kgBB.

5.2 Alur Penelitian Selanjutnya

1. Berdasarkan penelitian yang telah dilaksanakan, senyawa *O*-(asetil) parasetamol dapat dikembangkan menjadi obat baru.
2. Disarankan untuk melakukan studi lebih lanjut untuk mendapatkan data dan informasi yang lengkap, baik dari aspek farmakodinamika, farmakokinetika dan uji toksisitas, yakni hepatotoksik serta toksisitas kronik bila dibandingkan dengan pembanding parasetamol.

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LAMPIRAN A

SERTIFIKAT HEWAN COBA MENCIT (*MUS MUSCULUS*)

CV. SURABAYA MOUSE SERVICE

WEDORO MASJID NO. 20E, RT 01 RW 05 WARU SIDOARJO

Telp : 085731276778 - 087856677108

Yang bertanda tangan di bawah ini :

Nama : M. Syamsul Bahri S. kom

Selaku penanggung jawab pengembangan Hewan Percobaan

Menerangkan bahwa yang digunakan pada penelitian :

Judul	: Sintesis O- (Asetil) Paracetamol dan uji Aktivitas Analgesik terhadap mencit (Mus Musculus) dengan metode Hot Plate
Peneliti	: Milody Noviana
Fakultas	: Farmasi Widya Mandala Surabaya
NIM / NIP	: 2443010049

Merupakan hewan uji dengan spesifikasi :

Tikus galur	: Swiss Webster
Umur	: 2-3 bulan
Jenis kelamin	: Jantan
Jumlah	: 42 ekor

Demikian surat ini dibuat untuk digunakan sebaik – baiknya.

Sidoarjo, 11 november 2013

Penanggung jawab

M. Syamsul Bahri S. kom

LAMPIRAN B

PERHITUNGAN JUMLAH MENCIT YANG DIGUNAKAN

Rumus : $(n-1)(t-1) \geq 15$

Jumlah kelompok pengujian adalah 7 kelompok, maka dapat dihitung jumlah mencit minimal yang digunakan adalah :

$$(n-1)(7-1) \geq 15$$

$$(n-1)6 \geq 15$$

$$(n-1) \geq \frac{15}{6}$$

$$(n-1) \geq 2{,}5$$

$$n \geq 2{,}5 + 1$$

$$n \geq 3{,}5$$

LAMPIRAN C

SERTIFIKAT ANALISIS PARASETAMOL

FROM :PT BRATACO FAX NO. :0218934659 29 Apr. 2012 11:47PM P1

PT.BRATACO

HASIL PEMERIKSAAN

Nama Bahan	: Parasetamol
No Batch	: J 0920/11 (1009053)
Ex	: Hengshui Jiheng
E.D	: 09/2014
Grade	: farma

Jenis Pemeriksaan	*Persyaratan FI IV*	*Hasil*
Pemerian	Serbuk hablur,putih,tidak berbau, rasa pahit	sesuai
Kelarutan	Larut dalam air mendidih,mudah larut dalam etanol	sesuai
Suhu Lebur	$168^{0}C$ - $172^{0}C$	$169.3 - 170.3^{0}$ C
Susut Pengeringan	Tidak lebih dari 0,5%	0,2%
Kadar	98,0 % - 101,0%	99.5 %

Kesimpulan : Memenuhi Syarat

Cikarang, 28-09-2011

Penanggung Jawab

Pemeriksa

Tatang Suhartono

Analis

Dra. ... Apoteker

SIK 36387B

HEAD OFFICE : Jl. Cideng Barat No. 78, Jakarta Pusat 10150 Telp. (021) 3822733 (hunting) Fax. : (021) 3522734, E-mail : btcsak@brataco.com

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Jl. Boulevard Raya Blok TB2 No. 5, Jakarta 14240 Telp. (021) 45846692-94 Fax. (021) 4532815

• BANDUNG

LAMPIRAN D
PERHITUNGAN BERAT

1. Parasetamol = n x BM
   = 0,025 mol x 151,16 gr/mol
   = 3,779 gram

2. Asetil Klorida

= n x BM	BJ	= massa / volume
= 0,05 mol x 78,5 gr/mol	1,1	= 3,925 gram / vol
= 3,925 gram	volume	= 3,568 ml ≈ 3,6 ml

3. Pyridine

= n x BM	BJ	= massa / volume
= 0,05 mol x 79,10 gr/mol	0,9819	= 3,955 gram / vol
= 3,955 gram	volume	= 4,0279 ml ≈ 4,0 ml

LAMPIRAN E

PERHITUNGAN PERSENTASE HASIL SINTESIS SENYAWA *O*-(ASETIL)PARASETAMOL

Reaksi : $C_8H_9NO_2$ + CH_3COOCl → $C_{10}H_{11}NO_3$ + HCl

0,025 mol	0,05 mol		
0,025 mol	0,025 mol	0,025 mol	0,025 mol
-	0,025 mol	0,025 mol	0,025 mol

Berat teoritis senyawa *O*-(asetil)parasetamol = n x BM

= 0,025 mol x 193,20 gr/mol

= 4,83 gram

Persentase senyawa *O*-(asetil)parasetamol =

$$\frac{berat\ senyawa\ hasil\ sintesis}{berat\ senyawa\ teoritis}\ x\ 100\%$$

$$= \frac{3{,}0074\ gram}{4{,}83\ gram}\ x\ 100\%$$

= 62,2650%

LAMPIRAN F

HASIL PENGAMATAN WAKTU RESPON MENCIT TERHADAP STIMULASI PANAS PADA KELOMPOK PARASETAMOL DAN SENYAWA *O*-(ASETIL)PARASETAMOL

Senyawa Pembanding Parasetamol Dosis 50 mg/kgBB

Mencit	Waktu							Kumulatif
	0’	10’	20’	30’	40’	50’	60	
1	1,9	2,1	2,7	2,7	2,0	2,3	2,5	16,2
2	1,4	2,2	2,1	2,6	1,7	2,0	3,1	15,1
3	2,0	2,5	1,6	2,5	3,1	3,0	2,6	16,3
4	1,8	1,9	2,1	3,1	1,8	3,0	1,6	17,3
5	2,1	1,9	2,5	2,8	2,1	2,3	2,2	16,0
6	1,7	2,1	2,0	1,9	2,9	2,6	2,9	16,1
X ± SD								**16,16 ± 0,70**

Senyawa Pembanding Parasetamol Dosis 100 mg/kgBB

Mencit	Waktu							Kumulatif
	0’	10’	20’	30’	40’	50’	60	
1	2,3	4,1	3,4	2,5	2,0	1,9	2,2	18,4
2	2,1	2,9	2,0	2,9	2,1	3,3	2,7	17,4
3	2,0	2,9	2,5	2,6	3,7	2,7	2,4	18,8
4	1,9	3,4	3,2	3,3	2,7	2,9	2,6	20,0
5	2,0	3,4	3,0	2,3	1,9	2,8	3,0	18,4
6	1,6	1,8	2,4	3,0	2,4	2,8	2,2	16,2
X ± SD								**18,2 ± 1,28**

Senyawa Uji *O*-(Asetil)parasetamol Dosis 50 mg/kgBB

Mencit	Waktu							Kumulatif
	0’	10’	20’	30’	40’	50’	60	
1	1,7	1,9	2,5	2,4	2,6	2,7	2,5	16,3
2	2,0	2,2	2,9	3,8	2,7	1,5	2,2	17,3
3	2,2	3,4	3,1	2,0	1,8	2,0	2,4	16,9
4	2,1	2,5	2,6	1,9	2,2	2,7	2,8	16,8
5	2,3	2,2	2,1	2,8	1,5	3,4	2,7	17,0
6	2,4	2,4	2,9	2,4	2,6	2,2	2,5	17,4
X ± SD								**16,95 ± 0,70**

Senyawa Uji *O*-(Asetil)parasetamol Dosis 100 mg/kgBB

Mencit	Waktu							Kumulatif
	0’	10’	20’	30’	40’	50’	60	
1	2,0	3,4	3,2	2,5	2,4	3,0	3,7	20,2
2	2,1	2,0	2,7	2,7	3,0	2,2	2,9	17,6
3	1,9	3,1	2,3	3,6	2,0	3,1	2,5	18,5
4	1,6	2,5	3,0	3,1	2,6	3,0	2,5	18,3
5	2,0	3,1	2,7	3,0	2,7	2,9	2,4	18,8
6	2,5	3,4	2,7	2,3	2,8	3,0	3,5	20,3
X ± SD								**18,95 ± 1,33**

LAMPIRAN G

HASIL UJI *ONE WAY ANOVA* DAN UJI *TUKEY* HSD WAKTU RESPON MENCIT TERHADAP STIMULASI PANAS KELOMPOK PARASETAMOL DAN *O*-(ASETIL)PARASETAMOL

ANOVA

Waktu_respon

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	186.756	6	31.126	37.618	.000
Within Groups	28.960	35	.827		
Total	215.716	41			

Multiple Comparisons

Waktu_respon
Tukey HSD

(I) Senyawa	(J) Senyawa	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound

Kontrol	Parasetamol 25 mg	-3.15000*	.52518	.000	-4.7917	-1.5083
	Parasetamol 50 mg	-4.18333*	.52518	.000	-5.8250	-2.5417
	Paraetamol 100 mg	-6.21667*	.52518	.000	-7.8583	-4.5750
	O-(asetil) Parasetamol 25 mg	-4.56667*	.52518	.000	-6.2083	-2.9250
	O-(asetil) Parasetamol 50 mg	-4.96667*	.52518	.000	-6.6083	-3.3250
	O-(asetil) Parasetamol 100 mg	-6.96667*	.52518	.000	-8.6083	-5.3250
Parasetamol 25 mg	Kontrol	3.15000*	.52518	.000	1.5083	4.7917
	Parasetamol 50 mg	-1.03333	.52518	.452	-2.6750	.6083
	Paraetamol 100 mg	-3.06667*	.52518	.000	-4.7083	-1.4250
	O-(asetil) Parasetamol 25 mg	-1.41667	.52518	.129	-3.0583	.2250
	O-(asetil) Parasetamol 50 mg	-1.81667*	.52518	.022	-3.4583	-.1750
	O-(asetil) Parasetamol 100 mg	-3.81667*	.52518	.000	-5.4583	-2.1750
Parasetamol 50 mg	Kontrol	4.18333*	.52518	.000	2.5417	5.8250
	Parasetamol 25 mg	1.03333	.52518	.452	-.6083	2.6750
	Paraetamol 100 mg	-2.03333*	.52518	.007	-3.6750	-.3917
	O-(asetil) Parasetamol 25 mg	-.38333	.52518	.990	-2.0250	1.2583
	O-(asetil) Parasetamol 50 mg	-.78333	.52518	.748	-2.4250	.8583
	O-(asetil) Parasetamol 100 mg	-2.78333*	.52518	.000	-4.4250	-1.1417

Paraetamol 100 mg	Kontrol	6.21667*	.52518	.000	4.5750	7.8583
	Parasetamol 25 mg	3.06667*	.52518	.000	1.4250	4.7083
	Parasetamol 50 mg	2.03333*	.52518	.007	.3917	3.6750
	O-(asetil) Parasetamol 25 mg	1.65000*	.52518	.048	.0083	3.2917
	O-(asetil) Parasetamol 50 mg	1.25000	.52518	.237	-.3917	2.8917
	O-(asetil) Parasetamol 100 mg	-.75000	.52518	.783	-2.3917	.8917
O-(asetil) Parasetamol 25 mg	Kontrol	4.56667*	.52518	.000	2.9250	6.2083
	Parasetamol 25 mg	1.41667	.52518	.129	-.2250	3.0583
	Parasetamol 50 mg	.38333	.52518	.990	-1.2583	2.0250
	Paraetamol 100 mg	-1.65000*	.52518	.048	-3.2917	-.0083
	O-(asetil) Parasetamol 50 mg	-.40000	.52518	.987	-2.0417	1.2417
	O-(asetil) Parasetamol 100 mg	-2.40000*	.52518	.001	-4.0417	-.7583
O-(asetil) Parasetamol 50 mg	Kontrol	4.96667*	.52518	.000	3.3250	6.6083
	Parasetamol 25 mg	1.81667*	.52518	.022	.1750	3.4583
	Parasetamol 50 mg	.78333	.52518	.748	-.8583	2.4250
	Paraetamol 100 mg	-1.25000	.52518	.237	-2.8917	.3917
	O-(asetil) Parasetamol 25 mg	.40000	.52518	.987	-1.2417	2.0417
	O-(asetil) Parasetamol 100 mg	-2.00000*	.52518	.009	-3.6417	-.3583
O-(asetil)	Kontrol	6.96667*	.52518	.000	5.3250	8.6083

Parasetamol 100 mg	Parasetamol 25 mg	3.81667*	.52518	.000	2.1750	5.4583
	Parasetamol 50 mg	2.78333*	.52518	.000	1.1417	4.4250
	Paraetamol 100 mg	.75000	.52518	.783	-.8917	2.3917
	O-(asetil) Parasetamol 25 mg	2.40000*	.52518	.001	.7583	4.0417
	O-(asetil) Parasetamol 50 mg	2.00000*	.52518	.009	.3583	3.6417

*. The mean difference is significant at the 0.05 level.

Homogeneous Subsets

waktu_respon

Tukey HSD[a]

		Subset for alpha = 0.05				
Senyawa	N	1	2	3	4	5
Kontrol	6	11.9833				
parasetamol 25 mg/kgBB	6		15.1333			
parasetamol 50 mg/kgBB	6		16.1667	16.1667		

o-(asetil)parasetamol 25 mg/kgBB	6		16.5500	16.5500		
o-(asetil)parasetamol 50 mg/kgBB	6			16.9500	16.9500	
parasetamol 100 mg/kgBB	6				18.2000	18.2000
o-(asetil)parasetamol 100 mg/kgBB	6					18.9500
Sig.		1.000	.129	.748	.237	.783

Means for groups in homogeneous subsets are displayed.

a. Uses Harmonic Mean Sample Size = 6,000.

LAMPIRAN H

PERHITUNGAN PERSENTASE HAMBATAN NYERI KELOMPOK PARASETAMOL DAN SENYAWA *O*-(ASETIL)PARASETAMOL

$$\%\ Hambatan\ Nyeri\ =\ \frac{Tu - Tk}{Tk}\ x\ 100\%$$

Krterangan :

Tk = waktu respon panas rata-rata pada kelompok kontrol.

Tu = waktu respon panas rata-rata pada kelompok uji atau kelompok senyawa pembanding.

a. Parasetamol dosis 25 mg/kgBB

$$\%\ Hambatan\ Nyeri\ =\ \frac{15{,}13 - 11{,}98}{11{,}98}\ x\ 100\%$$

$$= 26{,}26\ \%$$

b. Parasetamol dosis 50 mg/kgBB

$$\%\ Hambatan\ Nyeri\ =\ \frac{16{,}16 - 11{,}98}{11{,}98}\ x\ 100\%$$

$$= 34{,}85\ \%$$

c. Parasetamol dosis 100 mg/kgBB

$$\%\ Hambatan\ Nyeri\ =\ \frac{18{,}23 - 11{,}98}{11{,}98}\ x\ 100\%$$

$$= 51{,}80\ \%$$

d. Senyawa *O*-(asetil)parasetamol dosis 25 mg/kgBB

$$\%\ Hambatan\ Nyeri\ =\ \frac{16{,}55 - 11{,}98}{11{,}98}\ x\ 100\%$$

$$= 38{,}11\ \%$$

e. Senyawa *O*-(asetil)parasetamol dosis 50 mg/kgBB

$$\%\ Hambatan\ Nyeri = \frac{16{,}95 - 11{,}98}{11{,}98}\ x\ 100\%$$

$$= 41{,}45\ \%$$

f. Senyawa *O*-(asetil)parasetamol dosis 100 mg/kgBB

$$\%\ Hambatan\ Nyeri = \frac{18{,}95 - 11{,}98}{11{,}98}\ x\ 100\%$$

$$= 58{,}14\ \%$$

LAMPIRAN I

ANALISA PROBIT SENYAWA PARASETAMOL DAN SENYAWA *O*-(ASETIL) PARASETAMOL

Parasetamol

Data Information

		N of Cases
Valid		3
Rejected	Missing	0
	Number of Responses > Number of Subjects	0
Control Group		0

Parameter Estimates

	Parameter		Estimate	Std. Error	Z	Sig.	95% Confidence Interval	
							Lower Bound	Upper Bound
PROBIT[a]	d i m e n s i o n 1	Dosis	,009	,002	3,770	,000	,004	,014
		Intercept	-,852	,162	-5,261	,000	-1,014	-,690

a. PROBIT model: PROBIT(p) = Intercept + BX

Cell Counts and Residuals

Number		Dosis	Number of Subjects	Observed Responses	Expected Responses	Residual	Probability
PROBIT	1	25,000	100	26	26,547	-,287	,265
	2	50,000	100	35	34,406	,444	,344

Cell Counts and Residuals

	Number	Dosis	Number of Subjects	Observed Responses	Expected Responses	Residual	Probability
PROBIT	1	25,000	100	26	26,547	-,287	,265
	2	50,000	100	35	34,406	,444	,344
	3	100,000	100	52	51,951	-,151	,520

Confidence Limits

	Probability	95% Confidence Limits for Dosis		
		Estimate	Lower Bound	Upper Bound
PROBIT	,010	-163,725	-407,228	-86,031
	,020	-133,458	-344,363	-65,941
	,030	-114,255	-304,508	-53,164
	,040	-99,810	-274,549	-43,530
	,050	-88,059	-250,198	-35,676
	,060	-78,058	-229,487	-28,974
	,070	-69,288	-211,343	-23,083
	,080	-61,436	-195,111	-17,794
	,090	-54,295	-180,363	-12,969
	,100	-47,722	-166,802	-8,514
	,150	-20,507	-110,867	10,142
	,200	1,123	-66,855	25,414
	,250	19,680	-29,819	39,237

,300	36,344	2,063	53,030
,350	51,786	28,755	68,661
,400	66,439	49,206	88,371
,450	80,615	64,200	112,233
,500	**94,568**	76,251	138,422
,550	108,520	87,044	165,870
,600	122,696	97,383	194,386
,650	137,349	107,719	224,211
,700	152,791	118,390	255,864
,750	169,456	129,752	290,176
,800	188,012	142,286	328,501
,850	209,642	156,798	373,273
,900	236,857	174,961	429,702
,910	243,430	179,336	443,343
,920	250,571	184,086	458,165
,930	258,423	189,304	474,468
,940	267,193	195,128	492,679
,950	277,194	201,764	513,455
,960	288,945	209,555	537,871
,970	303,390	219,125	567,894
,980	322,594	231,835	607,815
,990	352,860	251,848	670,757

O-(asetil)parasetamol

Data Information

		N of Cases
Valid		3
Rejected	Missing	0
	Number of Responses > Number of Subjects	0
Control Group		0

Parameter Estimates

						95% Confidence Interval	
	Parameter	Estimate	Std. Error	Z	Sig.	Lower Bound	Upper Bound
PROBIT[a]	Dosis	.007	.002	2.990	.003	.002	.012
	Intercept	-.514	.156	-3.299	.001	-.670	-.358

a. PROBIT model: PROBIT(p) = Intercept + BX

Cell Counts and Residuals

	Number	Dosis	Number of Subjects	Observed Responses	Expected Responses	Residual	Probability
PROBIT	1	25.000	100	38	36.745	1.365	.367
	2	50.000	100	41	43.521	-2.071	.435
	3	100.000	100	58	57.450	.690	.575

Confidence Limits

	Probability	95% Confidence Limits for Dosis		
		Estimate	Lower Bound	Upper Bound
PROBIT	.010	-258.179	-862.031	-131.742
	.020	-219.344	-749.431	-108.145
	.030	-194.704	-678.012	-93.151
	.040	-176.169	-624.301	-81.856
	.050	-161.092	-580.624	-72.657
	.060	-148.259	-543.458	-64.816

.070	-137.007	-510.880	-57.932
.080	-126.932	-481.720	-51.759
.090	-117.769	-455.208	-46.137
.100	-109.335	-430.812	-40.953
.150	-74.415	-329.925	-19.372
.200	-46.661	-249.968	-1.996
.250	-22.851	-181.689	13.228
.300	-1.469	-120.895	27.423
.350	18.344	-65.590	41.607
.400	37.146	-15.624	57.578
.450	55.336	25.573	80.177
.500	**73.238**	52.418	116.115
.550	91.140	69.504	161.813
.600	109.331	83.279	211.834
.650	128.132	96.150	264.901
.700	147.945	109.068	321.470

	.750	169.328	122.643	382.884
	.800	193.138	137.520	451.511
	.850	220.891	154.680	531.683
	.900	255.811	176.116	632.716
	.910	264.245	181.276	657.135
	.920	273.408	186.876	683.669
	.930	283.483	193.027	712.852
	.940	294.735	199.891	745.450
	.950	307.568	207.711	782.636
	.960	322.645	216.891	826.333
	.970	341.181	228.166	880.064
	.980	365.820	243.139	951.504
	.990	404.655	266.712	1064.128

LAMPIRAN J

TABEL KOLERASI (r)

Degrees of Freedom (DF)	5 Percent	1 Percent	Degrees of Freedom (DF)	5 Percent	1 Percent
1	.997	1.000	24	.388	.496
2	.950	.990	25	.381	.487
3	.878	.959	26	.374	.478
4	.811	.917	27	.367	.470
5	.754	.874	28	.361	.463
6	.707	.834	29	.355	.456
7	.666	.798	30	.349	.449
8	.632	.765	31	.325	.418
9	.602	.735	32	.304	.393
10	.576	.708	33	.288	.372
11	.553	.684	34	.273	.354
12	.532	.661	35	.250	.325
13	.514	.641	36	.232	.302
14	.497	.623	37	.217	.283
15	.482	.606	38	.205	.267
16	.468	.590	39	.195	.254
17	.456	.575	40	.174	.228
18	.444	.561	41	.159	.208
19	.433	.549	42	.138	.181
20	.423	.537	43	.113	.148
21	.413	.526	44	.098	.128
22	.404	.515	45	.088	.115
23	.396	.505	46	.062	.081

Sumber : Soediglo & Soedigdo, 1997

LAMPIRAN K

DOKUMENTASI PENELITIAN