DAFTAR PUSTAKA

Alassaf, M., & Qamar, A. M. (2022). Improving Sentiment Analysis of Arabic Tweets by One-way ANOVA. *Journal of King Saud University - Computer and Information Sciences*, *34*(6), 2849–2859. https://doi.org/10.1016/j.jksuci.2020.10.023

Amanullah, A., Upadhyay, A., Dhiman, R., Singh, S., Kumar, A., Ahirwar, D. K., Gutti, R. K., & Mishra, A. (2022). Development and Challenges of Diclofenac-Based Novel Therapeutics : Targeting Cancer and Complex Diseases. *Cancers*, *14*(18), 1–19. https://doi.org/https://doi.org/10.3390/cancers14184385

Amir, M. N., Aulia, R., Suardi, H., Hatifah, Z. A., Raihan, M., Evary, M., Farmasi, D., Farmasi, F., & Hasanuddin, U. (2023). Studi In Vivo Ekstrak Etanol Kulit Buah Nangka (Artocarpus heterophyllus L .) Sebagai Kandidat Obat Analgetik Terhadap Model Hewan Uji Mecit (Mus musculus). *Jurnal Mandala Pharmacon Indonesia (JMPI)*, *9*(1), 139–147.

Astuti, R. D., Khusna, K., & Pambudi, R. S. (2021). Gambaran Pengetahuan Mahasiswa Universitas Sahid Surakarta tentang Obat Generik. *Indonesian Journal of Pharmacy and Natural Product*, *04*(April), 107–112. http://repository.usahidsolo.ac.id/id/eprint/2075

Badan Pengawas Obat Dan Makanan Nomor 11 Tahun 2022 Tentang Tata Laksana Uji Bioekivalensi (2022).

Badan Pengawas Obat Dan Makanan Republik Indonesia Nomor 18 Tahun 2021 Tentang Pedoman Uji Farmakodinamik Praklinik Obat Tradisional, 1 (2021).

Bahrudin, M. (2017). Patofisiologi Nyeri. *Santika Medika: Jurnal Ilmu Kesehatan Dan Kedokteran Keluarga*, *13*(1), 7–13. https://doi.org/https://doi.org/10.22219/sm.v13i1.5449

Bindu, S., Mazumder, S., & Bandyopadhyay, U. (2020). Non-Steroidal Anti-inflammatory drugs (NSAIDs) and Organ Damage : A Current Perspective. *Biochemical Pharmacology*, *180*(July). https://doi.org/10.1016/j.bcp.2020.114147

Dewi, E. C., Sodik, A., Khuluq, H., Intiyani, R., & Tengah, J. (2023). EFEK ANALGETIK EKSTRAK AKUADES DAUN MELINJO (Gnetum gnemon L .) PADA MENCIT PUTIH (Mus musculus L .) JANTAN DENGAN

METODE INDUKSI ASAM ASETAT (Analgesic Effect of Melinjo Leaf Aquadest Extract (Gnetum gnemon L .) on Male White Mice (Mus musculus L .). *As-Syifaa Jurnal Farmasi*, *15*(2), 120–128. https://doi.org/https://doi.org/10.56711/jifa.v15i2.1055

Dureja, G. P., Iyer, R. N., Das, G., Ahdal, J., & Narang, P. (2017). Evidence and consensus recommendations for the pharmacological management of pain in India. *Journal of Pain Research*, *10*, 709–736. https://doi.org/https://doi.org/10.2147/JPR.S128655

Gunadi, E., & Istiana, T. (2024). Effective Pain Management in Patients. *Medula*, *14*(1).

Harfiansyah, M. D., Apulina, G., Purba, C., & Khairani, U. (2025). ORIGINAL ARTICLE Validation of an HPLC Analytical Method for the Determination of Paracetamol in Generic and Branded Tablet Dosage Forms Validasi Metode Analisis KCKT untuk Penetapan Kadar Parasetamol dalam Sediaan Tablet Generik dan Bermerek Abstrak. *Journal of Pharmaceutical and Sciences*, *1*(4), 3032–3038. https://doi.org/https://doi.org/10.36490/journal-jps.com.v8i4.1107

Hayati, R., Sari, A., & Chairunnisa, C. (2019). Formulasi spray gel ekstrak etil asetat Bunga Melati (Jasminum sambac (L.) Ait.) sebagai antijerawat. *Indonesian Journal of Pharmacy and Natural Product*, *2*(2). http:/jurnal.unw.ac.id/index.php/ijpnp

Keputusan Menteri Kesehatan Republik Indonesia Nomor Hk.01.07/MENKES/481/2019 Tentang Pedoman Nasional Pelayanan Kedokteran Tata Laksana Nyeri, 1 (2019).

Khairani, D., Ilyas, S., & Yurnadi. (2024). *Prinsip dan Praktik Hewan Percobaan Mencit (Mus musculus)*.

Kotowska-rodziewicz, A., Zalewska, A., & Maciejczyk, M. (2023). A Review of Preclinical and Clinical Studies in Support of the Role of Non-Steroidal Anti-Inflammatory Drugs in Dentistry. *Med Sci Monit*, *29*(e940635), 1–21. https://doi.org/10.12659/MSM.940635

Li, W., Li, X., He, Y., Shi, L., & Chen, J. (2025). Effects of Generic Entry on Market Shares and Prices of Originator Drugs : Evidence from Chinese Pharmaceutical Market. *PharmacoEconomics - Open*, *9*(4), 639–648. https://doi.org/10.1007/s41669-025-00570-6

Mobasheri, A., Pasqua, O. Della, Morlion, B., Sethi, V. S., & Cardosa, M. (2025). *Combination vs . single-drug nonprescription analgesics for acute pain management : A narrative review*. *June*, 2796–2816. https://doi.org/10.1002/bcp.70180

Muhammad Maulana Ma'sum. (2023). *Profil Penggunaan Asam Mefenamat dan Natrium Diklofenak pada Pasien Poli Gigi Bedah Mulut di RS Baladhika Husada Jember*.

Muliawan, C. (2019). Pemberian Paten Obat-obatan dan Pemenuhan Hak Asasi Manusia Terhadap Kesehatan di Indonesia. *Pranata Hukum*, *14*(2), 96–222.

Naresh, D. (2026). A Study on Comparison of Dissolution Profile Study of Immidiate-Release Diclofenak Sodium Tablets. *INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES*, *13*(01), 6–10. https://doi.org/https://doi.org/10.5281/zenodo.18140451

Nasif, H., Zaini, E., & Agnes, S. (2017). Uji Dissolusi Terbanding Tablet Metilprednisolon Generik Bermerek dan Generik Berlogo Dibandingkan Dengan Tablet Metilprednisolon Paten. *Jurnal Sains Dan Teknologi Farmasi*, *19*(Desember), 46–51.

Pinzon, R. T. (2016). *Pengkajian Nyeri*. Betha Grafika Yogyakarta.

Piva, M., Yaekashi, K. M., Pereira, T. G. O., Bertozzi, M. M., Camilios-Neto, D., Calixto-campos, C., Borghi, S. M., Zarpelon-schutz, A. C., & Fattori, V. (2026). Trans -Chalcone alleviates overt pain-like behavior by targeting the activation of nociceptive neuron TRPV1 and TRPA1 channels. *Inflammopharmacology*, 1–20. https://doi.org/https://doi.org/10.1007/s10787-025-02099-w

Purba, J. S. (2022). Peran Analgesik Nonsteroidal Anti-inflammatory Drugs (NSAIDs) dan Analgesik Non-NSAID dalam Penanganan Nyeri Nosiseptif. *Medical Review*, *35*(1), 51–54.

Rho, J., Son, H.-Y., Kim, S. H., & Suh, H. N. (2025). 13-Month Follow Up of Acclimation of Cynomolgus Macaques (Macaca fascicularis) on Haematology , Serum Biochemistry , and Body Weight Changes. *Journal of Medical Primatology*, *54*(6). https://doi.org/10.1111/jmp.70038

Rismen, S., & Lovia, L. (2023). Pendampingan Penggunaan Software SPSS dalam Pengolahan Data Statistik. *JURNAL ILMIAH PENGABDIAN DAN INOVASI*,

2(2), 433–442. https://doi.org/https://doi.org/10.57248/jilpi.v2i2.334

Santoso, F. K. N., Ansori1, M. M. L., Fitriani1, D., & PUSVETMA, B. B. V. F. (2023). Penerapan Kesejahteraan Hewan Serta Teknik dan Manajemen Pemeliharaan Mencit di BBVF PUSVETMA Surabaya. *Buletin Veteriner Farma*, *19*(2), 19–34.

Suhail, M., Wu, P., & Usman, M. (2021). Development and characterization of pH-sensitive chondroitin sulfate-co-poly (acrylic acid) hydrogels for controlled release of diclofenac sodium. *Journal of Saudi Chemical Society*, *25*. https://doi.org/10.1016/j.jscs.2021.101212

Sulung, S. T., Ahwan, & Qonitah, F. (2024). Perbandingan Efektivitas Analgesik Dua Sediaan Tablet Paracetamol Generik Dan Tablet Asam Mefenamat Generik Terhadap Mencit Putih Jantan (Mus Musculus) dengan Menggunakan Metode Geliat Sandi. *JFST : Jurnal Farmasi Sains Dan Kesehatan*, *2*(2), 83–90.

Suryaningsih, F., Syamsul, D., & Zubaidi, P. A. (2023). Pola Penggunaan Obat Analgetik Antiinflamasi Nonsteroid di Pelayanan Farmasi IGD. *Indah Sains Dan Klinis*, *04*(03), 12–17.

Ulubay, M., Yurt, K., Ahsen, A., & Kemal, M. (2018). The use of diclofenac sodium in urological practice : A structural and neurochemical based review. *Journal of Chemical Neuroanatomy*, *87*, 32–36. https://doi.org/10.1016/j.jchemneu.2017.02.005

Undang-Undang Republik Indonesia Nomor 65 Tahun 2024 Tentang Perubahan Ketiga Atas Undang-Undang Nomor 13 Tahun 2016 Tentang Paten (2024).

Vaegter, H. B., Støten, M., Silseth, S. L., Erlangsen, A., & Handberg, G. (2019). Observational study Cause-specific mortality of patients with severe chronic pain referred to a multidisciplinary pain clinic : a cohort register-linkage study. *Scandinavian Journal of Pain*, *19*(1), 93–99. https://doi.org/https://doi.org/10.1515/sjpain-2018-0094

LAMPIRAN

Lampiran 1 Etik Penelitian

YAYASAN HARAPAN BUNDA BATAM
INSTITUT KESEHATAN MITRA BUNDA
KOMITE ETIK PENELITIAN
Jl. Seraya No 1 KOTA BATAM Telp/Fax (0778) 429431, website : http:\\ikmb.ac.id
SURAT KEPUTUSAN MENTERI PENDIDIKAN DAN KEBUDAYAAN REPUBLIK INDONESIA No. 284/M/2020

KOMITE ETIK PENELITIAN
INSTITUT KESEHATAN MITRA BUNDA
THE RESEARCH ETHICAL COMMITTEE INSTITUT KESEHATAN MITRA BUNDA

SURAT KETERANGAN
ETHICAL APPROVAL
No. 029/K/KEP/IKMB/IV/2026

Komite Etik Penelitian Institut Kesehatan Mitra Bunda, menyatakan dengan ini bahwa penelitian dengan judul :
The Research Ethical Committee of Institut Kesehatan Mitra Bunda states hereby that the following proposal :

"Perbandingan Aktivitas Analgesik Natrium Diklofenak Originator Dengan Generik Model Nyeri Nosiseptif Pada Mencit (*Mus musculus*)"
"Comparison of the Analgesic Activity of Brand-Name and Generic Diclofenac Sodium in a Model of Nociceptive Pain in Mice (Mus musculus)"

Peneliti Utama : Muji Nur Ma'rifah
Principal Investigato

Lokasi Penelitian : Laboratorium Farmakologi dan Toksikologi
Research Location

Waktu Penelitian : April - Juli 2026
Time Schedule

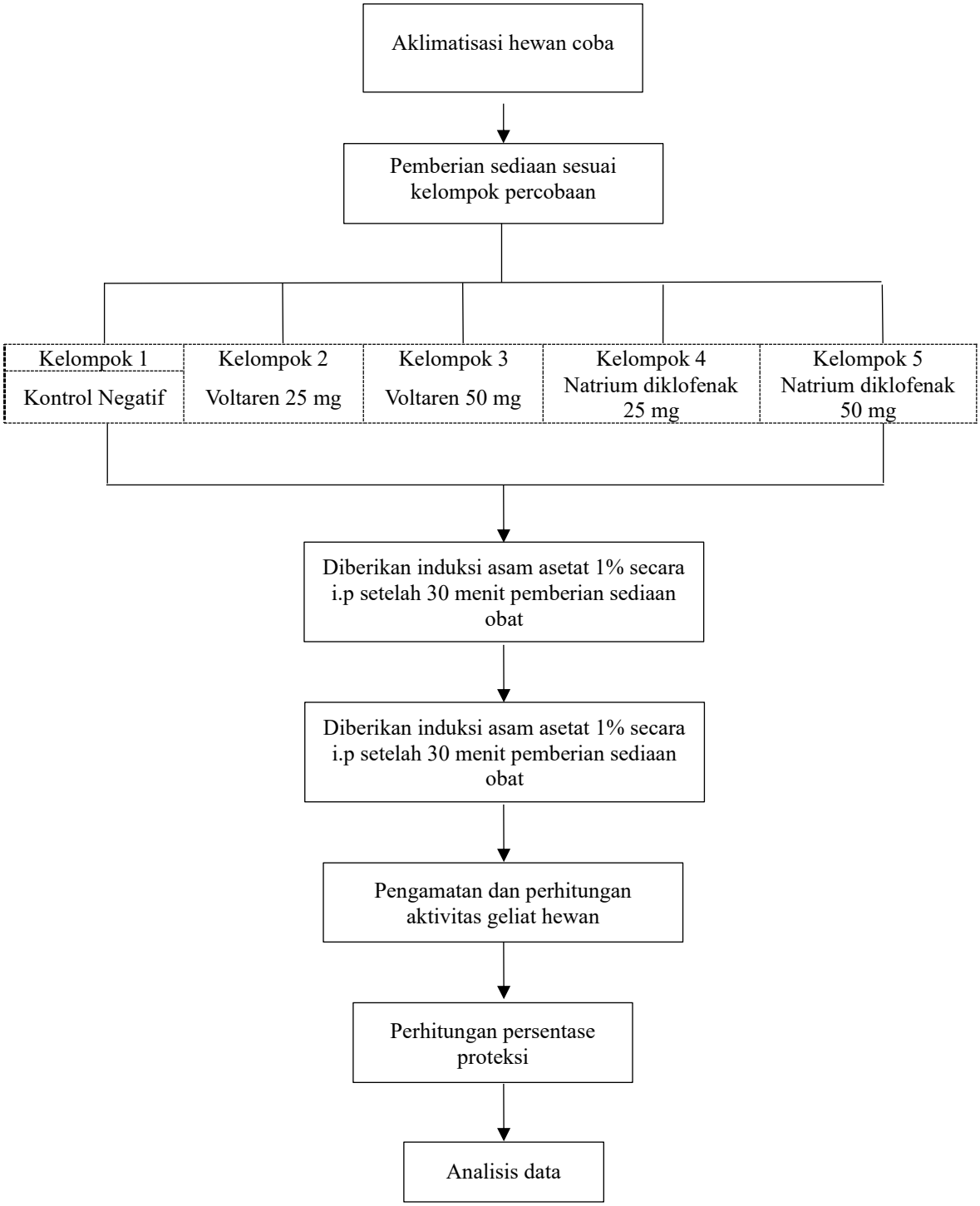
Responden/Subjek Penelitian : Hewan Percobaan (25 ekor mencit)
Respondent/Research Subject

Telah melalui prosedur kaji etik dan dinyatakan layak untuk dilaksanakan
Has proceeded the ethichal assessment procedure and been approved fot implementation

Batam, 29 April 2026
Ketua / *Chairman*,

dr. Ibnu Rushd, M.K.M

Lampiran 2 Skema Kerja



Lampiran 3 Perhitungan Populasi Percobaan

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

$$4(n-1) \geq 15$$

$$4n-4 \geq 15$$

$$4n \geq 15+4$$

$$4n \geq 19$$

$$n \geq 5$$

Lampiran 4 Perhitungan Dosis

1. Voltaren 25 mg
   a. Konversi

      Mencit 20 g =Dosis Lazim (mg)×Faktor Konversi
      =25 mg×0,0026
      =0,065 mg

      Mencit 28 g $=\frac{28\ g}{20\ g}\times 0{,}065=0{,}091$ mg

   b. Larutan stok

      $\frac{0{,}091\times 50\ ml}{0{,}5\ ml}=9{,}1$ mg

      Sediaan yang ditimbang:

      $\frac{150\ mg}{25\ mg}\times 9{,}1\ mg=54{,}6$ mg

   c. Dosis/BB Hewan

      – Mencit $1=\frac{24g}{28g}\times 0{,}091=0{,}077$
        $Vp=\frac{0{,}077}{0{,}091}\times 1\ ml=0{,}85$ ml
      – Mencit $2=\frac{28g}{28g}\times 0{,}091=0{,}091$
        $Vp=\frac{0{,}091}{0{,}091}\times 1\ ml=1$ ml
      – Mencit $3=\frac{21g}{28g}\times 0{,}091=0{,}068$
        $Vp=\frac{0{,}068}{0{,}091}\times 1\ ml=0{,}75$ ml
      – Mencit $4=\frac{21g}{28g}\times 0{,}091=0{,}068$
        $Vp=\frac{0{,}068}{0{,}091}\times 1\ ml=0{,}75$ ml
      – Mencit $5=\frac{21g}{28g}\times 0{,}091=0{,}068$
        $Vp=\frac{0{,}068}{0{,}091}\times 1\ ml=0{,}75$ ml

2. Voltaren 50 mg
   a. Konversi

      Mencit 20 g =Dosis Lazim (mg)×Faktor Konversi
      =50 mg×0,0026
      =0,13 mg

      Mencit 35 g $=\frac{35\ g}{20\ g}\times 0{,}13=0{,}22$

   b. Larutan stok

      $\frac{0{,}22\times 50ml}{0{,}5\ ml}=22$ mg

Sediaan yang ditimbang:

$$\frac{128mg}{50\ mg} \times 22\ mg = 95{,}92\ mg$$

c. Dosis/BB Hewan

- Mencit 1 $= \frac{32g}{35g} \times 0{,}22 = 0{,}20$

  $Vp = \frac{0{,}20}{0{,}22} \times 1\ ml = 0{,}90\ ml$
- Mencit 2 $= \frac{24g}{35g} \times 0{,}22 = 0{,}15$

  $Vp = \frac{0{,}15}{0{,}22} \times 1\ ml = 0{,}68\ ml$
- Mencit 3 $= \frac{35g}{35g} \times 0{,}22 = 0{,}22$

  $Vp = \frac{0{,}22}{0{,}22} \times 1\ ml = 1\ ml$
- Mencit 4 $= \frac{24g}{35g} \times 0{,}22 = 0{,}15$

  $Vp = \frac{0{,}15}{0{,}22} \times 1\ ml = 0{,}68\ ml$
- Mencit 5 $= \frac{28\ g}{35\ g} \times 0{,}22 = 0{,}176$

  $Vp = \frac{0{,}176}{0{,}22} \times 1\ ml = 0{,}8\ ml$

3. Natrium diklofenak 25 mg

a. Konversi

$$\text{Mencit 20 g} = \text{Dosis Lazim (mg)} \times \text{Faktor Konversi}$$
$$= 25\ mg \times 0{,}0026$$
$$= 0{,}065\ mg$$
$$\text{Mencit 30 g} = \frac{30\ g}{20\ g} \times 0{,}065 = 0{,}097$$

b. Larutan stok

$$\frac{0{,}097 \times 50\ ml}{0{,}5\ ml} = 9{,}7\ mg$$

Sediaan yang ditimbang:

$$\frac{88\ mg}{25\ mg} \times 9{,}7\ mg = 34{,}18\ mg$$

c. Dosis/BB Hewan

- Mencit 1 $= \frac{28\ g}{30\ g} \times 0{,}097 = 0{,}090$

  $Vp = \frac{0{,}090}{0{,}097} \times 1\ ml = 0{,}92\ ml$
- Mencit 2 $= \frac{23\ g}{30\ g} \times 0{,}097 = 0{,}074$

  $Vp = \frac{0{,}074}{0{,}097} \times 1\ ml = 0{,}76\ ml$
- Mencit 3 $= \frac{30\ g}{30\ g} \times 0{,}097 = 0{,}097$

$$Vp=\frac{0,097}{0,097}\times 1\text{ ml}=1\text{ ml}$$

- Mencit 4 $=\frac{20\text{ g}}{30\text{ g}}\times 0,097=0,064$

$$Vp=\frac{0,064}{0,097}\times 1\text{ ml}=0,65\text{ ml}$$

- Mencit 5 $=\frac{22\text{ g}}{30\text{ g}}\times 0,097=0,071$

$$Vp=\frac{0,071}{0,097}\times 1\text{ ml}=0,73\text{ ml}$$

4. Natriun diklofenak 50 mg

a. Konversi

Mencit 20 g = Dosis Lazim (mg) × Faktor Konversi

$$=50\text{ mg}\times 0,0026$$

$$=0,13\text{ mg}$$

$$\text{Mencit 33 g} = \frac{33\text{ g}}{20\text{ g}}\times 0,13=0,21$$

b. Larutan stok

$$\frac{0,21\times 50\text{ ml}}{0,5\text{ ml}}=21\text{ mg}$$

Sediaan yang ditimbang:

$$\frac{233\text{ mg}}{50\text{ mg}}\times 21\text{ mg}=97,86\text{ mg}$$

c. Dosis/BB Hewan

- Mencit 1 $=\frac{23\text{ g}}{33\text{ g}}\times 0,21=0,14$

$$Vp=\frac{0,14}{0,21}\times 1\text{ ml}=0,66\text{ ml}$$

- Mencit 2 $=\frac{24\text{ g}}{33\text{ g}}\times 0,21=0,15$

$$Vp=\frac{0,15}{0,21}\times 1\text{ ml}=0,72\text{ ml}$$

- Mencit 3 $=\frac{31\text{ g}}{33\text{ g}}\times 0,21=0,19$

$$Vp=\frac{0,19}{0,21}\times 1\text{ ml}=0,93\text{ ml}$$

- Mencit 4 $=\frac{33\text{ g}}{33\text{ g}}\times 0,21=0,21$

$$Vp=\frac{0,21}{0,21}\times 1\text{ ml}=1\text{ ml}$$

- Mencit 5 $=\frac{27\text{ g}}{33\text{ g}}\times 0,21=0,17$

$$Vp=\frac{0,17}{0,21}\times 1\text{ ml}=0,81\text{ ml}$$

Lampiran 5 Kegiatan Penelitian

No	Gambar	Perlakuan
1		Aklimatisasi hewan uji
2	 	Obat yang digunakan
3		Penimbangan sediaan obat
4		Serbuk sediaan obat

No	Gambar	Perlakuan
4		Pembuatan sediaan suspensi
5		Pemberian sediaan larutan obat secara oral
6		Pemberian larutan asam asetat secara intraperitoneal
7		Pengamatan aktivitas geliat hewan uji selama 60 menit

Lampiran 6 Data Hasil Perlakuan Hewan Uji

Obat	Hewan Perlakuan	Menit Perlakuan												Jumlah
		5	10	15	20	25	30	35	40	45	50	55	60	
Negatif	1	15	30	40	36	37	39	29	23	29	27	19	17	341
	2	5	34	27	30	23	25	24	20	15	15	12	11	241
	3	15	29	23	20	19	16	19	24	14	12	14	11	216
	4	1	30	25	20	20	15	35	10	5	3	4	10	178
	5	15	35	21	14	11	20	12	20	25	28	17	13	231
Voltaren 25mg	1	6	20	29	21	16	12	12	12	9	7	3	3	150
	2	0	32	47	68	43	30	28	18	13	11	7	0	297
	3	4	15	23	20	20	13	5	8	4	0	2	0	114
	4	29	44	40	35	32	16	19	15	16	13	15	13	287
	5	2	15	18	13	12	8	11	8	4	3	2	3	99
Natrium Diklofenak 25mg	1	0	5	41	25	19	35	27	11	8	10	8	0	189
	2	0	35	34	37	27	22	10	10	10	8	10	7	210
	3	10	15	24	27	28	30	33	30	36	30	41	43	347
	4	0	7	17	18	16	18	15	15	8	15	11	12	152
	5	0	10	8	19	18	17	12	17	11	14	20	33	179
Voltaren 50mg	1	2	19	11	11	8	13	9	6	7	6	4	7	103
	2	3	18	20	14	7	10	7	6	9	11	8	9	122
	3	0	18	13	12	10	9	13	9	7	12	7	6	116
	4	1	30	32	32	24	17	14	12	16	11	7	13	209
	5	6	24	19	10	16	8	12	8	11	12	7	16	149
Natrium Diklofenak 50mg	1	3	4	14	15	8	9	11	8	8	6	10	17	113
	2	0	16	35	23	22	12	9	22	12	9	16	30	206
	3	0	8	5	17	20	19	16	10	10	3	1	1	110
	4	0	15	25	20	20	17	11	12	10	8	5	5	148
	5	1	46	42	22	15	13	12	11	12	8	7	6	195

Lampiran 7 Perhitungan Persentase Proteksi Hewan Coba

1. Originator (Voltaren 25 mg)

$$\%Proteksi = 100\% - ({}^{P}/_{K} \times 100\%)$$

$$\%Proteksi = 100\% - ({}^{189,40}/_{241,40} \times 100\%)$$

$$\%Proteksi = 100\% - 78{,}4\%$$

$$\%Proteksi = 21{,}5\%$$

2. Originator (Voltaren 50 mg)

$$\%Proteksi = 100\% - ({}^{P}/_{K} \times 100\%)$$

$$\%Proteksi = 100\% - ({}^{139,80}/_{241,40} \times 100\%)$$

$$\%Proteksi = 100\% - 57{,}9\%$$

$$\%Proteksi = 42{,}0\%$$

3. Generik (Natrium Diklofenak 25 mg)

$$\%Proteksi = 100\% - ({}^{P}/_{K} \times 100\%)$$

$$\%Proteksi = 100\% - ({}^{215,40}/_{241,40} \times 100\%)$$

$$\%Proteksi = 100\% - 89{,}2\%$$

$$\%Proteksi = 10{,}7\%$$

4. Generik (Natrium Diklofenak 50 mg)

$$\%Proteksi = 100\% - ({}^{P}/_{K} \times 100\%)$$

$$\%Proteksi = 100\% - ({}^{154,40}/_{241,40} \times 100\%)$$

$$\%Proteksi = 100\% - 63{,}9\%$$

$$\%Proteksi = 36{,}0\%$$

Lampiran 8 Hasil Analisis Data Statistik

Tests of Normality

	Kelompok perlakuan	Kolmogorov-Smirnov[a] Statistic	df	Sig.	Shapiro-Wilk Statistic	df	Sig.
Jumlah geliat	Negatif	.303	5	.151	.890	5	.358
	Voltaren 25	.260	5	.200*	.823	5	.123
	Voltaren 50	.264	5	.200*	.865	5	.246
	Nadik 25	.328	5	.083	.803	5	.086
	Nadik 50	.222	5	.200*	.870	5	.264

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Test of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Jumlah geliat	Based on Mean	1.828	4	20	.163
	Based on Median	.666	4	20	.623
	Based on Median and with adjusted df	.666	4	14.325	.626
	Based on trimmed mean	1.688	4	20	.192

ANOVA

Jumlah geliat

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	35282.240	4	8820.560	1.966	.139
Within Groups	89743.600	20	4487.180		
Total	125025.840	24			