

DAFTAR PUSTAKA

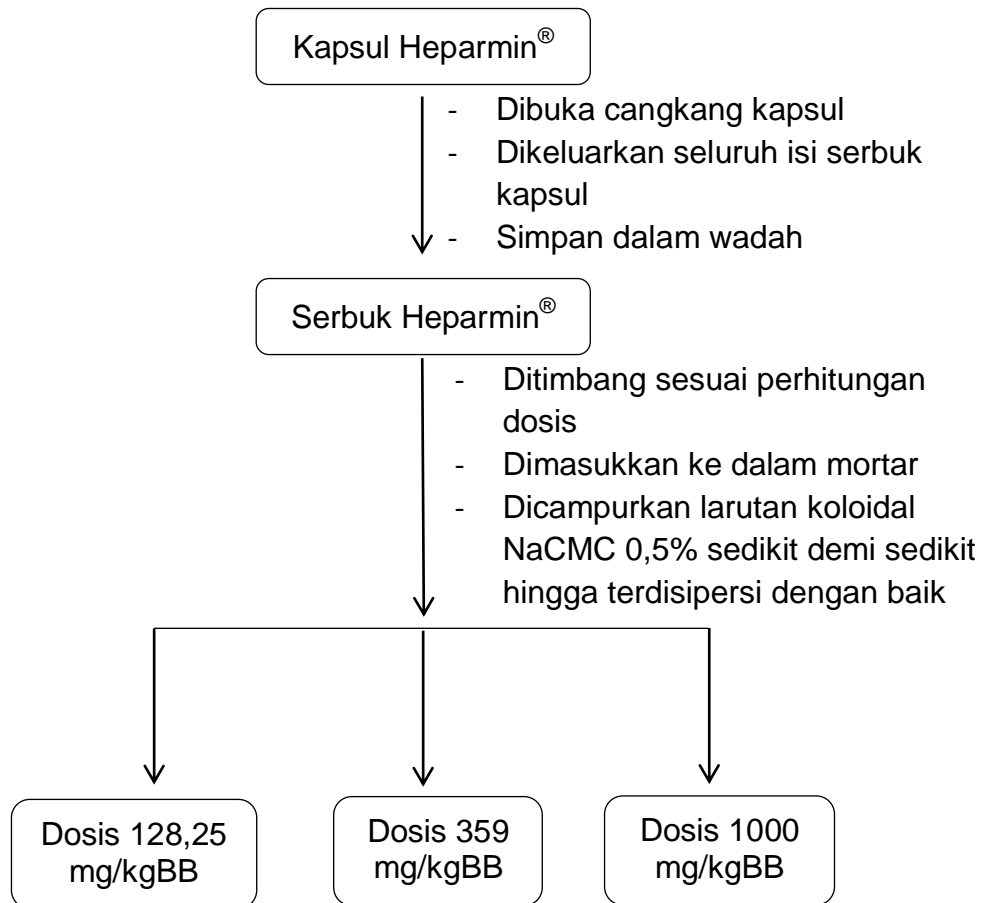
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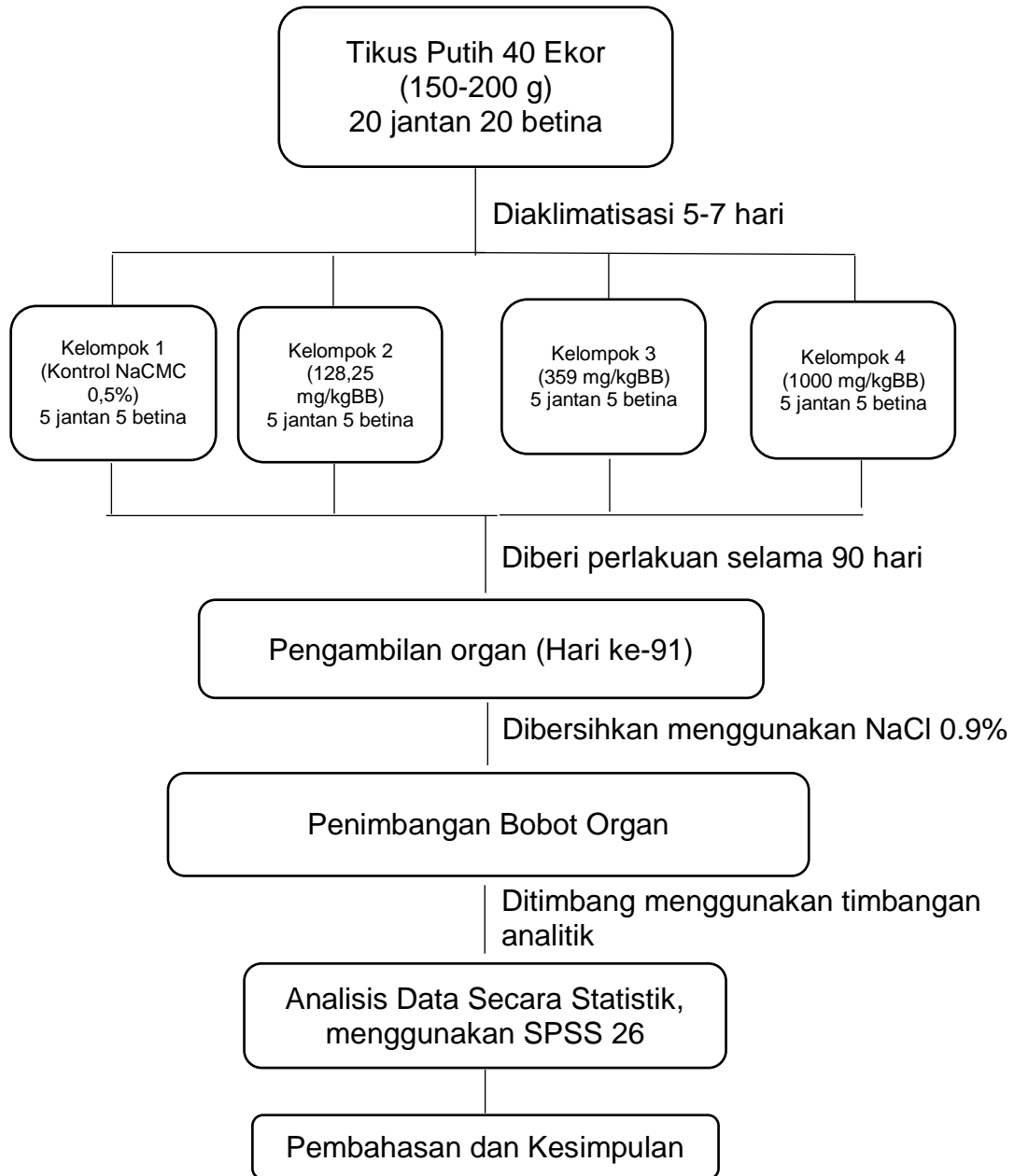
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LAMPIRAN

Lampiran 1. Skema Pembuatan Suspensi Isi Kapsul Heparmin[®]



Lampiran 2. Skema Perlakuan Uji dan Analisis Data

Keterangan :

- Kelompok 1 (Kontrol NaCMC 0,5%) : Hewan uji diberikan pakan standar + larutan koloidal NaCMC 0,5% secara per oral (dimulai dari hari 1 hingga hari ke-90)
- Kelompok 2 (Perlakuan 1) : Hewan uji diberikan pakan standar + suspensi Heparmin[®] 128,25 mg/kgBB secara per oral (dimulai hari ke 1 hingga hari ke-90).
- Kelompok 3 (Perlakuan 2) : Hewan uji diberi pakan pakan standar + suspensi Heparmin[®] 359 mg/kgBB secara per oral (dimulai hari ke 1 hingga hari ke-90).
- Kelompok 4 (Perlakuan 3) : Hewan uji diberi pakan pakan standar + suspensi Heparmin[®] 1000 mg/kgBB secara per oral (dimulai hari ke 1 hingga hari ke-90).

Lampiran 3. Perhitungan Dosis

1. NaCMC 0,5% $= \frac{0,5 \text{ g}}{100 \text{ mL}} \times 1000 \text{ mL} = 5 \text{ g}$ (ditimbang)
= 1000 mL (air suling)
2. Dosis 128,25 mg/kgBB = 128,25 mg/kgBB
= 25,65 mg/200 gBB/2 mL
= 6412,5 mg/500 mL
= 6,4125 g/500 mL
3. Dosis 359 mg/kgBB = 359 mg/kgBB
= 7180 mg/200 gBB/2 mL
= 17950 mg/500 mL
= 17,95 g/500 mL
4. Dosis 1000 mg/kgBB = 1000 mg/kgBB
= 200 mg/200 gBB/2 mL
= 50000 mg/500 mL
= 50 g/500 mL

Lampiran 4. Data Hasil Analisis Statistik

Lampiran 4.1 Organ Jantung

Lampiran 4.1.1 Tikus Jantan

Uji Normalitas

	Perlakuan	Tests of Normality					
		Kolmogorov-Smirnov ^a			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Indeks Organ	NaCMC	.198	5	.200	.951	5	.742
Jantung Tikus	Dosis 1	.200	5	.200	.935	5	.627
Jantan	Dosis 2	.290	5	.195	.869	5	.263
	Dosis 3	.242	5	.200	.893	5	.370

*. This is a lower bound of the true significance.
a. Lilliefors Significance Correction

Uji Homogenitas

Test of Homogeneity of Variances					
		Levene Statistic	df1	df2	Sig.
Indeks Organ	Based on Mean	1.316	3	16	.304
Jantung Tikus	Based on Median	.450	3	16	.721
Jantan	Based on Median and with adjusted df	.450	3	12.419	.722
	Based on trimmed mean	1.315	3	16	.304

One Way Anova

ANOVA					
Indeks Organ Jantung Tikus Jantan					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.002	3	.001	.293	.830
Within Groups	.031	16	.002		
Total	.033	19			

Post Hoc

Multiple Comparisons	
Dependent Variable: Indeks Organ Jantung Tikus Jantan	
Games-Howell	

(I) Perlakuan	(J) Perlakuan	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
NaCMC	Dosis 1	-.00600	.02182	.992	-.0774	.0654
	Dosis 2	-.02000	.02514	.854	-.1048	.0648
	Dosis 3	-.02200	.02814	.860	-.1195	.0755
Dosis 1	NaCMC	.00600	.02182	.992	-.0654	.0774
	Dosis 2	-.01400	.02786	.956	-.1040	.0760
	Dosis 3	-.01600	.03059	.951	-.1166	.0846
Dosis 2	NaCMC	.02000	.02514	.854	-.0648	.1048
	Dosis 1	.01400	.02786	.956	-.0760	.1040
	Dosis 3	-.00200	.03305	1.000	-.1083	.1043
Dosis 3	NaCMC	.02200	.02814	.860	-.0755	.1195
	Dosis 1	.01600	.03059	.951	-.0846	.1166
	Dosis 2	.00200	.03305	1.000	-.1043	.1083

Lampiran 4.1.2 Tikus Betina

Uji Normalitas

	Perlakuan	Tests of Normality					
		Kolmogorov-Smirnov ^a			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Indeks Organ Jantung Tikus Betina	NaCMC	.300	5	.161	.922	5	.543
	Dosis 1	.184	5	.200	.944	5	.692
	Dosis 2	.232	5	.200	.963	5	.825
	Dosis 3	.221	5	.200	.902	5	.421

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

a. Lilliefors Significance Correction

Uji Homogenitas

Test of Homogeneity of Variances				
	Levene Statistic	df1	df2	Sig.

Indeks Organ Jantung Tikus Betina	<i>Based on Mean</i>	2.417	3	16	.104
	<i>Based on Median</i>	1.225	3	16	.333
	<i>Based on Median and with adjusted df</i>	1.225	3	7.922	.363
	<i>Based on trimmed mean</i>	2.412	3	16	.105

One Way Anova

ANOVA					
Indeks Organ Jantung Tikus Betina					
	Sum of Squares	df	Mean Square	F	Sig.
<i>Between Groups</i>	.006	3	.002	1.579	.233
<i>Within Groups</i>	.019	16	.001		
Total	.025	19			

Post Hoc

Multiple Comparisons						
Dependent Variable: Indeks Organ Jantung Tikus Betina						
Games-Howell						
(I)	(J)	Mean	Std.	Sig.	95% Confidence Interval	
Perlakuan	Perlakuan	Difference (I-J)	Error		Lower Bound	Upper Bound
NaCMC	Dosis 1	.03000	.01844	.419	-.0298	.0898
	Dosis 2	-.00800	.02800	.991	-.1023	.0863
	Dosis 3	.02800	.01562	.370	-.0285	.0845
Dosis 1	NaCMC	-.03000	.01844	.419	-.0898	.0298
	Dosis 2	-.03800	.02653	.528	-.1313	.0553
	Dosis 3	-.00200	.01281	.998	-.0464	.0424
Dosis 2	NaCMC	.00800	.02800	.991	-.0863	.1023
	Dosis 1	.03800	.02653	.528	-.0553	.1313
	Dosis 3	.03600	.02466	.526	-.0593	.1313
Dosis 3	NaCMC	-.02800	.01562	.370	-.0845	.0285
	Dosis 1	.00200	.01281	.998	-.0424	.0464
	Dosis 2	-.03600	.02466	.526	-.1313	.0593

Lampiran 4.2 Organ Hati

Lampiran 4.2.1 Tikus Jantan

Uji Normalitas

		Tests of Normality					
		<i>Kolmogorov-Smirnov^a</i>			<i>Shapiro-Wilk</i>		
	Perlakuan	<i>Statistic</i>	<i>df</i>	<i>Sig.</i>	<i>Statistic</i>	<i>df</i>	<i>Sig.</i>
Indeks Organ Hati Tikus Jantan	NaCMC	.212	5	.200	.939	5	.657
	Dosis 1	.216	5	.200	.946	5	.707
	Dosis 2	.287	5	.200	.800	5	.082
	Dosis 3	.210	5	.200	.959	5	.804

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

a. Lilliefors Significance Correction

Uji Homogenitas

		Test of Homogeneity of Variances				
		<i>Levene</i>	<i>df1</i>	<i>df2</i>	<i>Sig.</i>	
		<i>Statistic</i>				
Indeks Organ Hati Tikus Jantan	<i>Based on Mean</i>	2.585	3	16	.089	
	<i>Based on Median</i>	2.357	3	16	.110	
	<i>Based on Median and with adjusted df</i>	2.357	3	7.232	.155	
	<i>Based on trimmed mean</i>	2.493	3	16	.097	

One Way Anova

ANOVA					
Indeks Organ Hati Tikus Jantan					
	<i>Sum of Squares</i>	<i>df</i>	<i>Mean Square</i>	<i>F</i>	<i>Sig.</i>
<i>Between Groups</i>	.531	3	.177	3.637	.036
<i>Within Groups</i>	.779	16	.049		
Total	1.311	19			

Post Hoc

Multiple Comparisons

Dependent Variable: Indeks Organ Hati Tikus Jantan

Tukey HSD

(I) Perlakuan	(J) Perlakuan	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
NaCMC	Dosis 1	-.04400	.13957	.989	-.4433	.3553
	Dosis 2	.01200	.13957	1.000	-.3873	.4113
	Dosis 3	-.38400	.13957	.062	-.7833	.0153
Dosis 1	NaCMC	.04400	.13957	.989	-.3553	.4433
	Dosis 2	.05600	.13957	.977	-.3433	.4553
	Dosis 3	-.34000	.13957	.110	-.7393	.0593
Dosis 2	NaCMC	-.01200	.13957	1.000	-.4113	.3873
	Dosis 1	-.05600	.13957	.977	-.4553	.3433
	Dosis 3	-.39600	.13957	.052	-.7953	.0033
Dosis 3	NaCMC	.38400	.13957	.062	-.0153	.7833
	Dosis 1	.34000	.13957	.110	-.0593	.7393
	Dosis 2	.39600	.13957	.052	-.0033	.7953

Lampiran 4.2.2 Tikus Betina

Uji Normalitas

	Perlakuan	Tests of Normality					
		Kolmogorov-Smirnov ^a			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Indeks Organ Hati Tikus Betina	NaCMC	.302	5	.155	.802	5	.085
	Dosis 1	.244	5	.200	.952	5	.749
	Dosis 2	.196	5	.200	.968	5	.860
	Dosis 3	.359	5	.034	.784	5	.060

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

a. Lilliefors Significance Correction

Uji Homogenitas

Test of Homogeneity of Variances					
		<i>Levene Statistic</i>	df1	df2	Sig.
Indeks Organ Hati Tikus Betina	<i>Based on Mean</i>	1.740	3	16	.199
	<i>Based on Median</i>	.670	3	16	.583
	<i>Based on Median and with adjusted df</i>	.670	3	7.046	.597
	<i>Based on trimmed mean</i>	1.362	3	16	.290

One Way Anova

ANOVA					
Indeks Organ Hati Tikus Betina					
	<i>Sum of Squares</i>	df	<i>Mean Square</i>	F	Sig.
<i>Between Groups</i>	.339	3	.113	2.364	.110
<i>Within Groups</i>	.764	16	.048		
Total	1.103	19			

Post Hoc

Multiple Comparisons						
<i>Dependent Variable: Indeks Organ Hati Tikus Betina</i>						
<i>Games-Howell</i>						
(I) Perlakuan	(J) Perlakuan	<i>Mean Difference (I-J)</i>	<i>Std. Error</i>	<i>Sig.</i>	<i>95% Confidence Interval</i>	
					<i>Lower Bound</i>	<i>Upper Bound</i>
NaCMC	Dosis 1	-.17200	.07676	.199	-.4241	.0801
	Dosis 2	-.31200	.10011	.059	-.6361	.0121
	Dosis 3	-.32000	.17356	.352	-.9524	.3124
Dosis 1	NaCMC	.17200	.07676	.199	-.0801	.4241
	Dosis 2	-.14000	.08990	.461	-.4459	.1659
	Dosis 3	-.14800	.16787	.815	-.7888	.4928
Dosis 2	NaCMC	.31200	.10011	.059	-.0121	.6361
	Dosis 1	.14000	.08990	.461	-.1659	.4459
	Dosis 3	-.00800	.17976	1.000	-.6382	.6222
Dosis 3	NaCMC	.32000	.17356	.352	-.3124	.9524
	Dosis 1	.14800	.16787	.815	-.4928	.7888
	Dosis 2	.00800	.17976	1.000	-.6222	.6382

Lampiran 4.3 Organ Ginjal

Lampiran 4.3.1 Tikus Jantan

Uji Normalitas

		Tests of Normality						
		Perlakuan	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
			Statistic	df	Sig.	Statistic	df	Sig.
Indeks Organ Ginjal Tikus Jantan	NaCMC		.245	5	.200	.906	5	.443
	Dosis 1		.162	5	.200	.959	5	.803
	Dosis 2		.263	5	.200	.875	5	.287
	Dosis 3		.259	5	.200	.888	5	.345

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

a. Lilliefors Significance Correction

Uji Homogenitas

		Test of Homogeneity of Variances				
			Levene Statistic	df1	df2	Sig.
Indeks Organ Ginjal Tikus Jantan	Based on Mean		.117	3	16	.949
	Based on Median		.081	3	16	.969
	Based on Median and with adjusted df		.081	3	14.369	.969
	Based on trimmed mean		.114	3	16	.951

One Way Anova

		ANOVA				
		Indeks Organ Ginjal Tikus Jantan				
		Sum of Squares	df	Mean Square	F	Sig.
	Between Groups	.016	3	.005	.970	.431
	Within Groups	.087	16	.005		
	Total	.103	19			

Post Hoc

		Multiple Comparisons	
		Dependent Variable: Indeks Organ Ginjal Tikus Jantan	

<i>Games-Howell</i>						
(I)	(J)	Mean	Std. Error	Sig.	95% Confidence Interval	
Perlakuan	Perlakuan	Difference (I-J)			Lower Bound	Upper Bound
NaCMC	Dosis 1	-.01000	.04785	.996	-.1640	.1440
	Dosis 2	.02600	.04622	.940	-.1238	.1758
	Dosis 4	-.05200	.05034	.736	-.2132	.1092
Dosis 1	NaCMC	.01000	.04785	.996	-.1440	.1640
	Dosis 2	.03600	.04250	.831	-.1003	.1723
	Dosis 4	-.04200	.04695	.808	-.1928	.1088
Dosis 2	NaCMC	-.02600	.04622	.940	-.1758	.1238
	Dosis 1	-.03600	.04250	.831	-.1723	.1003
	Dosis 4	-.07800	.04528	.375	-.2243	.0683
Dosis 4	NaCMC	.05200	.05034	.736	-.1092	.2132
	Dosis 1	.04200	.04695	.808	-.1088	.1928
	Dosis 2	.07800	.04528	.375	-.0683	.2243

Lampiran 4.3.2 Tikus Betina

Uji Normalitas

Tests of Normality							
	Perlakuan	<i>Kolmogorov-Smirnov^a</i>			<i>Shapiro-Wilk</i>		
		Statistic	df	Sig.	Statistic	df	Sig.
Indeks Organ Ginjal Tikus Betina	NaCMC	.221	5	.200	.915	5	.501
	Dosis 1	.231	5	.200	.869	5	.263
	Dosis 2	.212	5	.200	.932	5	.613
	Dosis 4	.289	5	.199	.890	5	.356

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

a. Lilliefors Significance Correction

Uji Homogenitas

Test of Homogeneity of Variances				
	Levene Statistic	df1	df2	Sig.

Indeks Organ Ginjal	<i>Based on Mean</i>	1.465	3	16	.261
Tikus Betina	<i>Based on Median</i>	.930	3	16	.449
	<i>Based on Median and with adjusted df</i>	.930	3	10.393	.460
	<i>Based on trimmed mean</i>	1.440	3	16	.268

One Way Anova

ANOVA

Indeks Organ Ginjal Tikus Betina					
	Sum of Squares	df	Mean Square	F	Sig.
<i>Between Groups</i>	.006	3	.002	.487	.696
<i>Within Groups</i>	.063	16	.004		
Total	.069	19			

Post Hoc

Multiple Comparisons

Dependent Variable: Indeks Organ Ginjal Tikus Betina

Games-Howell

(I)	(J)	Mean	Std.	Sig.	95% Confidence Interval	
Perlakuan	Perlakuan	Difference (I- J)	Error		Lower Bound	Upper Bound
NaCMC	Dosis 1	-.02400	.02946	.846	-.1296	.0816
	Dosis 2	-.04000	.03630	.704	-.1751	.0951
	Dosis 4	.00000	.03519	1.000	-.1303	.1303
Dosis 1	NaCMC	.02400	.02946	.846	-.0816	.1296
	Dosis 2	-.01600	.04379	.982	-.1580	.1260
	Dosis 4	.02400	.04287	.941	-.1146	.1626
Dosis 2	NaCMC	.04000	.03630	.704	-.0951	.1751
	Dosis 1	.01600	.04379	.982	-.1260	.1580
	Dosis 4	.04000	.04783	.836	-.1132	.1932
Dosis 4	NaCMC	.00000	.03519	1.000	-.1303	.1303
	Dosis 1	-.02400	.04287	.941	-.1626	.1146
	Dosis 2	-.04000	.04783	.836	-.1932	.1132

Lampiran 5. Dokumentasi Penelitian



Gambar 8. Penyiapan Hewan uji



Gambar 9. Produk Heparmin®



Gambar 10. Pembuatan Larutan Koloidal NaCMC 0,5%



Gambar 11. Pembuatan Suspensi Isi Kapsul Heparmin®



Gambar 12. Proses Pemberian Heparmin® terhadap Hewan uji



Gambar 13. Proses Hewan uji Dieutanasia



Gambar 14. Pembedahan Hewan Uji





Gambar 15. Penimbangan Bobot Organ



Gambar 16. Organ Hewan uji

Lampiran 6. Rekomendasi Persetujuan Etik




 KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
 UNIVERSITAS HASANUDDIN FAKULTAS KEDOKTERAN
 KOMITE ETIK PENELITIAN UNIVERSITAS HASANUDDIN
 RSPTN UNIVERSITAS HASANUDDIN
 RSUP Dr. WAHIDIN SUDIROHUSODO MAKASSAR
 Sekretariat : Lantai 2 Gedung Laboratorium Terpadu
 JL.PERINTIS KEMERDEKAAN KAMPUS TAMALANREA KM.10 MAKASSAR 90245.
 Contact Person: dr. Agusalim Bukhari, MMed,PhD, SpGK TELP. 081241850858, 0411 5780103. Fax : 0411-581431
 

REKOMENDASI PERSETUJUAN ETIK

Nomor : B10/UN4.6.4.5.31/ PP36/ 2022

Tanggal: 12 Desember 2022

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH22110704		No Sponsor Protokol	
Peneliti Utama	Venturini Vernanda Kombong Kila		Sponsor	
Judul Peneliti	Uji Toksisitas Subkronik Produk Herbal Hepatoprotektor (Heparmin®) terhadap Bobot Organ Jantung, Hati, dan Ginjal Tikus Putih (Rattus Norvegicus)			
No Versi Protokol	1	Tanggal Versi	16 Nopember 2022	
No Versi PSP			Tanggal Versi	
Tempat Penelitian	Laboratorium Fakultas Farmasi Universitas Hasanuddin Makassar			
Jenis Review	<input type="checkbox"/> Exempted <input checked="" type="checkbox"/> Expedited <input type="checkbox"/> Fullboard Tanggal		Masa Berlaku 12 Desember 2022 sampai 12 Desember 2023	Frekuensi review lanjutan
Ketua KEP Universitas Hasanuddin	Nama Prof.Dr.dr. Suryani As'ad, M.Sc.,Sp.GK (K)	Tanda tangan		
Sekretaris KEP Universitas Hasanuddin	Nama dr. Agusalim Bukhari, M.Med.,Ph.D.,Sp.GK (K)	Tanda tangan		

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan Laporan SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- Melaporkan penyimpangan dari protokol yang disetujui (protocol deviation / violation)
- Mematuhi semua peraturan yang ditentukan