DAFTAR PUSTAKA

1. Japaries, W. Karsinoma Pankreas. Dalam Buku Ajar Onkologi Klinis. Edisi Kedua. Jakarta. Balai Penerbit FK UI.2008: Hal 442-9

2. Mayer, J.R. Pancreatic Cancer. In: Kasper L, Denis *et al.* Harri-son's Principles of Internal Medicine .16th Edition. United States of America: McGraww Hill Companies, Inc. 2005; Chapter 79.Hal 446

3. Castillo, C.F., Jimenez.,Ramon, E. Pancreatic cancer. In: Feldman, M.,Friedman,L.S.,Brandt,L.J. Sleisenger & Fordtran's Gastro-intestinal and Liver Disease. 8th edition. Philadelphia. Elsevier, Inc. 2006. Chapter 58.Hal 3178

4. Padmomarono, F.S. Kanker Pankreas. In: Sudoyo, A.W dkk. Buku Ajar Ilmu Penyakit Dalam. Edisi Keempat. Jakarta: Interna Publishing. 2006; Hal 492-6

5. Lindseth, N.G. Gangguan hati, Kandung Empedu, dan Pankreas. In: Price, Sylvia A., Wilson, Lorraine M. Patofisiologi Edisi 6 Volume 1. Jakarta. Penerbit EGC. 2003; Hal 507-8

6. Hariharan, D., Saied, A., Kocher, H. Analysis of mortality rates for pancreatic cancer across the world. The Official Journal of the International Hepato Pancreato Biliary Association. Blackwell Publishing**.** Available from *www.ncbi.nlm.nih.gov*,updated december 20, 2007.Hal 58-62

7. Kim, M., Miyamoto, S., Yasui.Y., Oyama, T ., Murakami, A., Tanaka, T. Zerumbone, a tropical ginger sesquiterpene, inhibits colon and lung carcinogenesis in mice. *International Journal of Cancer.* 2009; 124 (2):Hal 264–271

8. Hasoya,T .,*et al.* "naturally Occurring Small Molecule Inhibitors of Hedgehog / GLI-Mediated transcription. Chembiochem, Vol.9,2008, Hal 1082-1092

9. Rubin, L.L. de Sanvage, F.J.Nat. Rev.Drug Disc.2006.5.Hal 1026

10. Rifai, Y ., *et al.* "A New Method For fast Isolation of GLI Inhibitory Compounds". *international journal of pharma research and review.*2012(8). Hal 28-30

11. Rifai, Y., Aswad, M., Subehan, " A New lignin From *Piper nigrum* fruit", Accepted in : *International Journal of Chemical and analytical Science*, will be published on November 2012.

12. Kitayama,T., *et al.* The Chemistry of Zerumbone IV Asymmetric Synthesis of Zerumbol.Juornal of Molecular Catalysis B:Enzymatic Volume 17.Hal 75-79

13. Takada, Y., Murakami, A., Aggarwal, B.B. Zerumbone abolishes NF-κB dan IκBα kinase activation leading to suppression of antiapoptotic dan metastatic gene expression, upregulation of apoptosis, and down regulation of invasion oncogene.2005; Hal. 6957-6969

14. Prakash, R.O., Rabinarayan, A., Kumar, M.S. *Zingiber zerumbet* (L.) Sm., a reservoir plant for therapeutic uses. IJPWR. 2011 Mar-Jun. 2 (2); Hal 1-23

15. Guyton, A.C. Textbook of Medical Physiology 5th Edition. WB Saunders Company: Philadelphia. London.1976. Hal 625-627

16. Gibson, J. Modern Physiology and Anatomy for Nurses. Blackwell Science Limited: Oxford. Chapter 19. 1981. Hal 241-247

17. Sundler, F., Hakanson, R. Peptide hormone producing endocrine or paracrine cell in the gastro- entero-pancreatic region. In : Handbook of Chemical Neuroanatomy**.** Vol.6: The Peripheral Nervous System. A Bjorklund, T. Hokfelt and C. Owman (eds). *Elsevier Science Publishers BV*. 1988. Hal 579-591

18. Meyer, B.N. Brine Shrimp : A Convenient General Bioassay for Active Plant Constituent. Drug Infor J. 1982. Vol. 32. Hal 513-524

19. Lewis, H.W., Lewis.E.M. “Medical Botany: Plants Affecting Man's Health”. John Wiley & Sons, Inc. United States of America*.*1997. Hal. 341

20. Bustan, M.N. “Epidemologi Penyakit Tidak Menular”. Rikena Cipta*.* Jakarta. 1999.Hal 234

21. Desen, W. Buku Ajar Onkologi Klinis edisi 2, Balai Penerbit FKUI, Jakarta. Hal 442-444

22. Abraham, J., Allegra,C. Bethesda Handbook of Clinical Oncology. Lippincott, Williams & Wilkins, New York. 2001. Hal 375-386

23. Bergamaschi, D., Samuels, Y., Jin, B., Puraisingham, S., Crook, T., Lu, X. ASPP1 dan ASPP2: Common Activators of p53 Family Members, Mol Cell Biol. 2004. Chapter 24. Hal 1341 – 1350

24. Masfarlane, M., Williams, A.C. Apoptosis and Desease: A Life or Death Decision, EMBO Rep. 2004. Hal 674 – 678

25. Raff, M., 1998, Cell Suicide for Beginners, Nature, 396:Hal 119-122

26. Sahakira, H., Enari, M., Nagata,S. Cleavage of CAD Inhibitor in CAD Activation and DNA Degradation During Apoptosis, Nature.1999. 391 (6662). Hal 96-99

27. Povlsen, C.O., Rygaard, J: Heterotransplantation of human epi-dermoid carcinomas to the mouse mutant nude. Acta Pathol Microbiol Scand.1972. 80(6): Hal 713-7

28. Steel, G.G., Courtenay, V.D., Peckham, M.J: The response to chemo-therapy of a variety of human tumour xenografts. *Br J Cancer* .1983. 47(1):Hal 1-13

29. Fiebig, H.H., Maier,A., Burger, A.M. Clonogenic assay with establish-ed human tumour xenografts: correlation of in vitro to in vivo activity as a basis for anticancer drug discovery. *Eur J Cancer*. 2004. 40(6): Hal 802-20

30. Kelland, L.R. Of mice and men: values and liabilities of the athymic nude mouse model in anticancer drug development. *Eur J Cancer.* 2004. 40(6): Hal 827-36

31. Killion, J.J., Radinsky, R., Fidler, I.J. Orthotopic models are necessary to predict therapy of transplantable tumors in mice. *Cancer Metastasis Rev*.1998. 17(3):Hal 279-84

32. Suggitt, M., Bibby, M.C. 50 years of preclinical anticancer drug screening: empirical to target-driven approaches. *Clin Cancer Res.* 2005. 11(3): Hal 971-81

33. Kerbel, R.S. Human tumor xenografts as predictive preclinical models for anticancer drug activity in humans: better than commonly perceived-but they can be improved.*Cancer Biol Ther .* 2003. 2(4 Suppl 1): Hal 134-9

34. Tan, MH., Holyoke, E.D., Goldrosen, M.H. Murine colon adeno-carcino-ma : syngeneic orthotopic transplantation ansubsequent hepatic metastases. J Nat Cancer Inst .1977. 59(5): Hal 1537-44

35. Bibby, M.C. Orthotopic models of cancer for preclinical drug evaluation: advantages and disadvantages. *Eur J Cancer*. 2004. 40(6): Hal 852-7

36. Fidler, I.J., Ellis, L.M. The implications of angiogenesis for the biology and therapy of cancer metastasis.1994. 79(2): Hal 185-8

37. McMahon, A.P., Ingham, P.W., Tabin, C. "Developmental Roles and Clinical Significance of Hedgehog Signaling". *J. Curr. Top. Dev. Biol.* 2003; vol.53. Hal.1

38. Rubin, L.L., Sauvage, D.F. "Novel Hedgehog Pathway Targets Agains Basal Cell Carcinoma". *J. Nat. Rev. Drug Disc*. 2006. vol.5: Hal. 1026

39. Kinzler ,K.W : vogelstem, B.Mol.Cell.Biol.1990.Vol.10:Hal. 634

40. (a)Magliano. M.P.D., Hebrok,M. Nat.Rev.Cancer 2003.3.903 : (b)Jacob, L.,Lum,L. science.2007.318.66:(c)taylor. M.D., Liu, L., raffle, C., hui., Hog, D.Nat.Genet.2002.Vol.37:Hal 306

41. Adityo, S. Kajian farmakologi Molekuler : Gemcitabine sebagai induktor apoptosis pada sel kanker Pankreas. 2008. Hal 9-12

42. Malgorzata, S., Milena, S., Magdalena, J., Alina, P., Danuta, P. Biological and physicochemical characterization of siRNAs modified with2′,2′-difluoro-2′-deoxycytidine (gemcitabine). 2010. Chapter 34.Hal : 918-924

43. Leeson, C.R., Leeson, T.S., Paparo,A. Buku Teks Histologi. Yan Tambayong.EGC. Jakarta. 1996. Hal 161-162

44. Tambajong, J. Sinopsis Histologi Edisi IX. Binarupa Aksara. Jakarta. 1995. Hal 258-260

45. Hoffbrand, A.V., Peffit, J.E., Moss,H. Kapita Selektif Hematologi Edisi 4. EGC. Jakarta. 2005. Hal 104-108

46. Cormach, D.H. Ham Histologi Edisi IX. Binarupa aksara. Jakarta. 1994. Hal 258 – 260

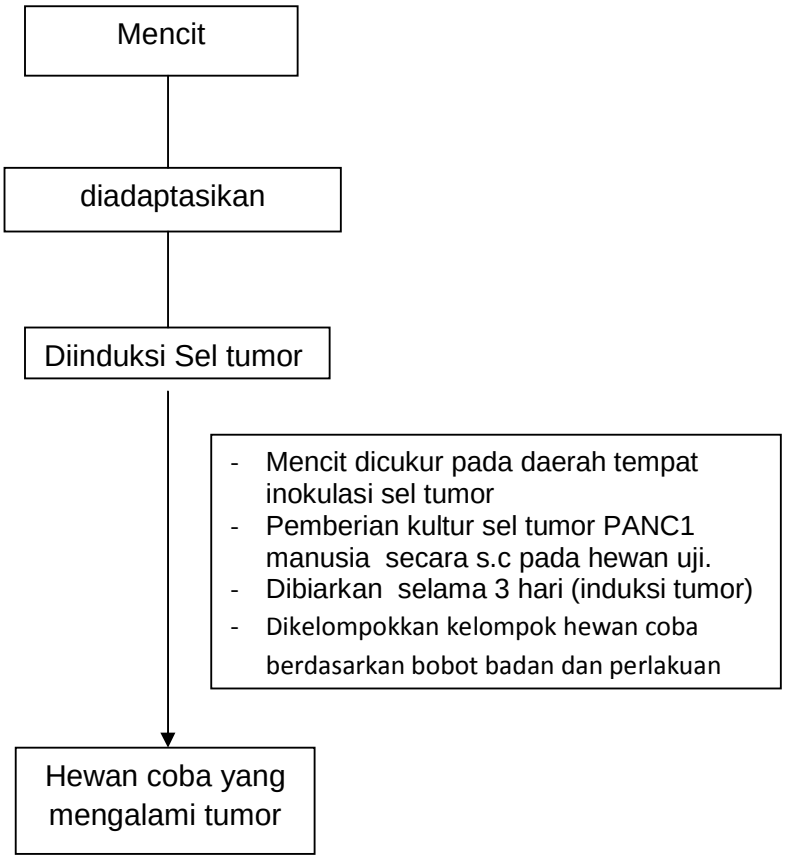
47. Baratawijaya, K.G. Imunologi Dasar Edisi Ke-7. Balai PenerbitFKUI. Jakarta. 2006. Hal 231,234

48. Malole, M.B.M., Pramono. Penggunaan Hewan Percobaan di Laboratorium. In: Setyadi, A.D. Organ Reproduksi dan Kualitas Sperma Mencit (*Mus musculus*) yang mendapat pakan Tambahan Kemangi (*Ocimum basilicum*) Segar. Institut Pertanian Bogor, Bogor. 1989. Hal 3-4

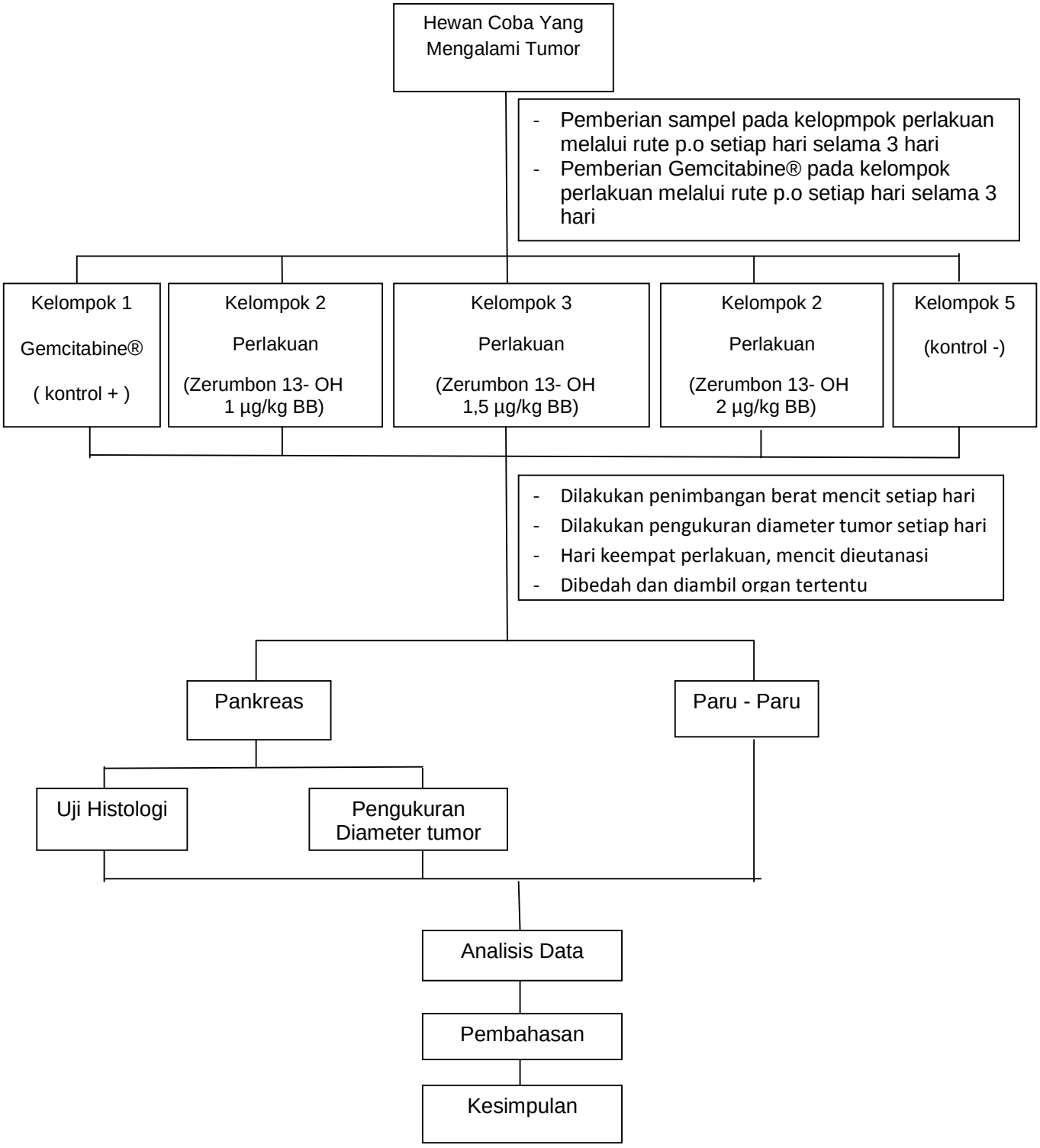
LAMPIRAN I

SKEMA KERJA

Skema Inokulasi Sel kanker PANC1



Skema Uji Efektifitas Derivat Zerumbon



LAMPIRAN II

PERHITUNGAN DOSIS

a. Perhitungan Pengenceran sampel

6 mg Zerumbon 13-OH ⟶ 15 mL suspensi NaCMC

↓

5 mL (2 mg Zerumbon 13-OH)

Pembuatan larutan stok Zerumbon 13-OH

5 mL (2 mg Zerumbon 13-OH) ⟶ 100 mL NaCMC (0,02 mg/mL)

b. Perhitungan Pengenceran Gemcitabine®

Dosis Gecitabin 40 mg/kg BB mencit

c. Perhitungan dosis sampel

$$\text{konversi dosis berdasarkan BB} = \text{Dosis (mg) x berat mencit (mg)}$$

$$\text{Volume Pemberian} = \frac{\text{Mr senyawa x konversi dosis (mg)}}{\text{konsentrasi senyawa } (\frac{\text{mg}}{\text{mL}})}$$

Mr Derivat Zerumbon 13-OH = 221

Konsentrasi senyawa = 0,02 mg/mL

- Kelompok perlakuan 1 (1µg/kg BB)

1. BB mencit 27 g

Konversi dosis = 10^{-3} mg x 27/1000 mg = 2,7 x 10^{-5} mg

$$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}000027 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}30 \text{ mL}$$

2. BB mencit 32 g

   Konversi dosis = 10^{-3} mg x 32/1000 mg = 3,2 x 10^{-5} mg

   $$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}000032 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}35 \text{ mL}$$

3. BB mencit 34 g

   Konversi dosis = 10^{-3} mg x 34/1000 mg = 3,4 x 10^{-5} mg

   $$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}000034 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}37 \text{ mL}$$

- Kelompok perlakuan 2 (1,5 µg/kg BB)

1. BB mencit 24 g

   Konversi dosis = 1,5.10^{-3} mg x 24/1000 mg = 3,6 x 10^{-5} mg

   $$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}000036 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0,40 \text{ mL}$$

2. BB mencit 26 g

   Konversi dosis = 1,5.10^{-3} mg x 26/1000 mg = 3,9 x 10^{-5} mg

   $$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}000039 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}43 \text{ mL}$$

3. BB mencit 28 g

   Konversi dosis = 1,5.10^{-3} mg x 26/1000 mg = 4,2 x 10^{-5} mg

   $$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}000042 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}46 \text{ mL}$$

- Kelompok perlakuan 3 (2 µg/kg BB)

1. BB mencit 33 g

Konversi dosis = 2.10^{-3} mg x 33/1000 mg = 6,6 x 10^{-5} mg

$$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}000066 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}72 \text{ mL}$$

2. BB mencit 30 g

Konversi dosis = 2.10^{-3} mg x 30/1000 mg = 6 x 10^{-5} mg

$$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}00006 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}67 \text{ mL}$$

3. BB mencit 30 g

Konversi dosis = 2.10^{-3} mg x 30/1000 mg = 6 x 10^{-5} mg

$$\text{Volume Pemberian} = \frac{221 \text{ x } 0{,}00006 \text{ mg}}{0{,}02 \text{ mg/mL}} = 0{,}67 \text{ mL}$$

LAMPIRAN III

PERHITUNGAN STATISTIK

Descriptives

Perlakuan	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Zerumbone 13 –OH 1	3	0,1867	0,03786	0,02186	0,0926	0,2807	0,16	0,23
Zerumbone 13 –OH 1,5	3	0,2100	0,02646	0,01528	0,1443	0,2757	0,18	0,23
Zerumbone 13 –OH 2	3	0,2933	0,03786	0,02186	0,1993	0,3874	0,25	0,32
Kontrol+	3	0,2200	0,02000	0,01155	0,1703	0,2697	0,20	0,24
Kontrol-	3	-0,0333	0,01155	0,00667	-0,0620	-0,0046	-0,04	-0,02
Total	15	0,1753	0,11667	0,03012	0,1107	0,2399	-0,04	0,32

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	0,182	4	0,046	55,602	0,000
Within Groups	0,008	10	0,001		
Total	0,191	14			

Multiple Comparisons

	(I) Perlakuan	(J) Perlakuan	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
LSD	Zerumbone 13 –OH 1	Zerumbone 13 –OH 1,5	-0,02333	0,02338	0,342	-0,0754	0,0288
		Zerumbone 13 –OH 2	-0,10667*	0,02338	0,001	-0,1588	-0,0546
		Kontrol+	-0,03333	0,02338	0,184	-0,0854	0,0188
		Kontrol-	0,22000*	0,02338	0,000	0,1679	0,2721
	Zerumbone13 –OH 1,5	Zerumbone13 –OH 1	0,02333	0,02338	0,342	-0,0288	0,0754
		Zerumbone13 –OH 2	-0,08333*	0,02338	0,005	-0,1354	-0,0312
		Kontrol+	-0,01000	0,02338	0,678	-0,0621	0,0421
		Kontrol-	0,24333*	0,02338	0,000	0,1912	0,2954
	Zerumbone13 –OH 2	Zerumbone13 –OH 1	0,10667*	0,02338	0,001	0,0546	0,1588
		Zerumbone13 –OH 1,5	0,08333*	0,02338	0,005	0,0312	0,1354
		Kontrol+	0,07333*	0,02338	0,011	0,0212	0,1254
		Kontrol-	0,32667*	0,02338	0,000	0,2746	0,3788
	Kontrol+	Zerumbon13 –OH e1	0,03333	0,02338	0,184	-0,0188	0,0854
		Zerumbone13 –OH 1,5	0,01000	0,02338	0,678	-0,0421	0,0621
		Zerumbone13 –OH 2	-0,07333*	0,02338	0,011	-0,1254	-0,0212
		Kontrol-	0,25333*	0,02338	0,000	0,2012	0,3054
	Kontrol-	Zerumbone13 –OH 1	-0,22000*	0,02338	0,000	-0,2721	-0,1679
		Zerumbone13 –OH 1,5	-0,24333*	0,02338	0,000	-0,2954	-0,1912
		Zerumbone13 –OH 2	-0,32667*	0,02338	0,000	-0,3788	-0,2746
		Kontrol+	-0,25333*	0,02338	0,000	-0,3054	-0,2012

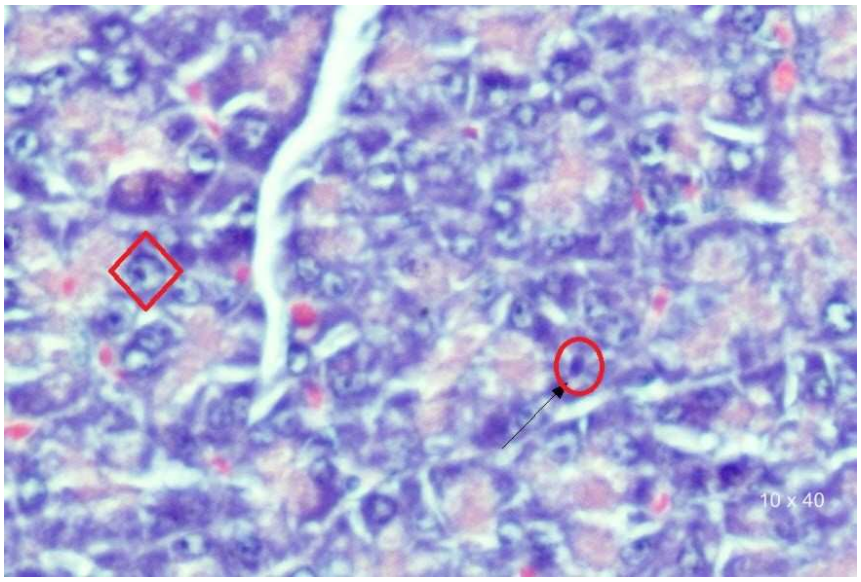
* signifikan pada taraf 0,05

Hasil

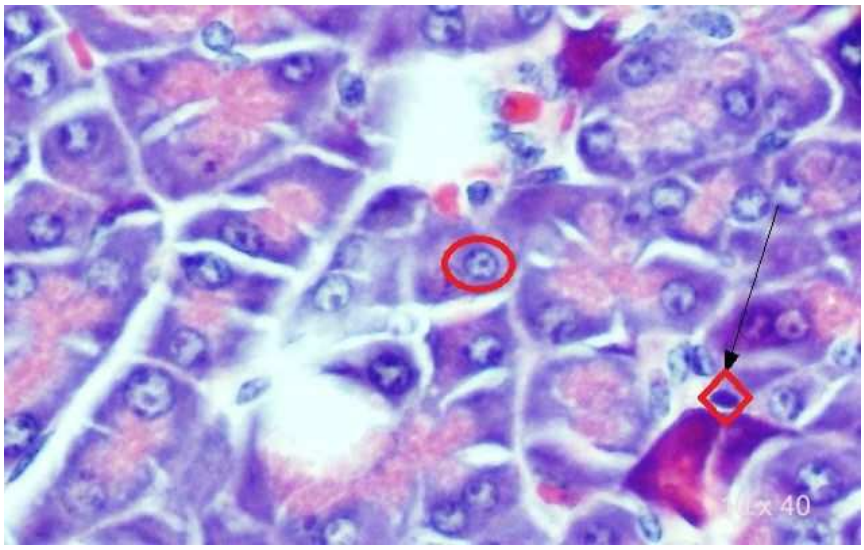
			Subset for alpha = 0.05		
	Perlakuan	N	1	2	3
Duncan[a]	Kontrol-	3	-0,0333		
	Zerumbone 13 –OH 1	3		0,1867	
	Zerumbone 13 –OH 1,5	3		0,2100	
	Kontrol+	3		0,2200	
	Zerumbone 13 –OH 2	3			0,2933
	Sig.		1.000	0,203	1.000

LAMPIRAN IV

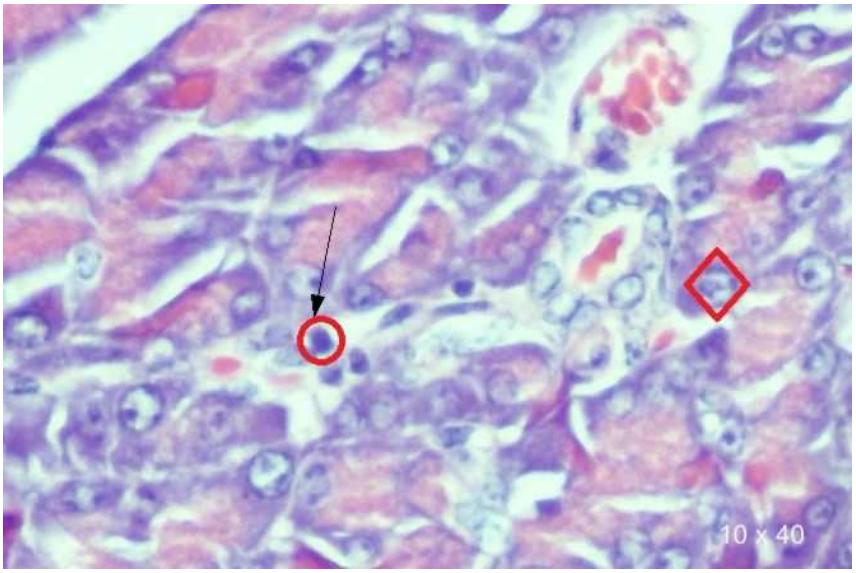
HASIL HISTOLOGI



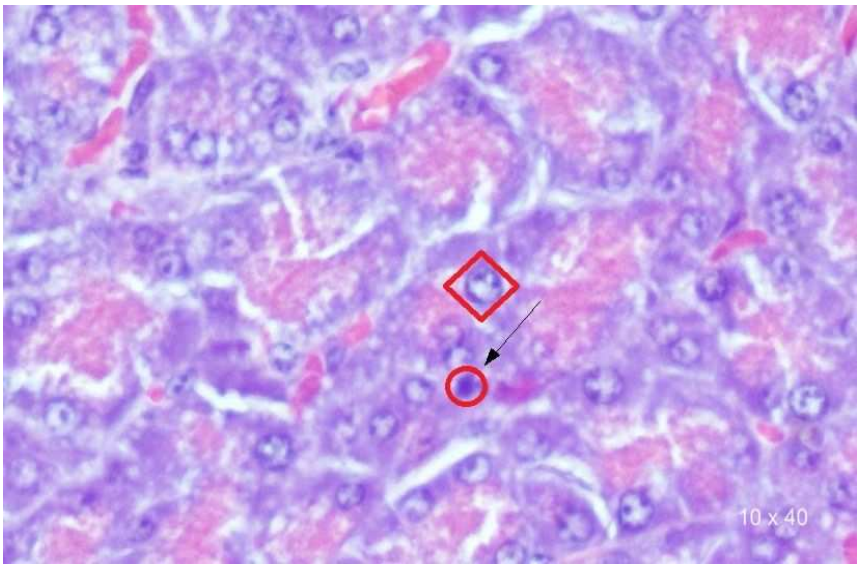
Gambar 10. Foto Histologi Pankreas (Zerumbon 13-OH 1 µg/kg BB)



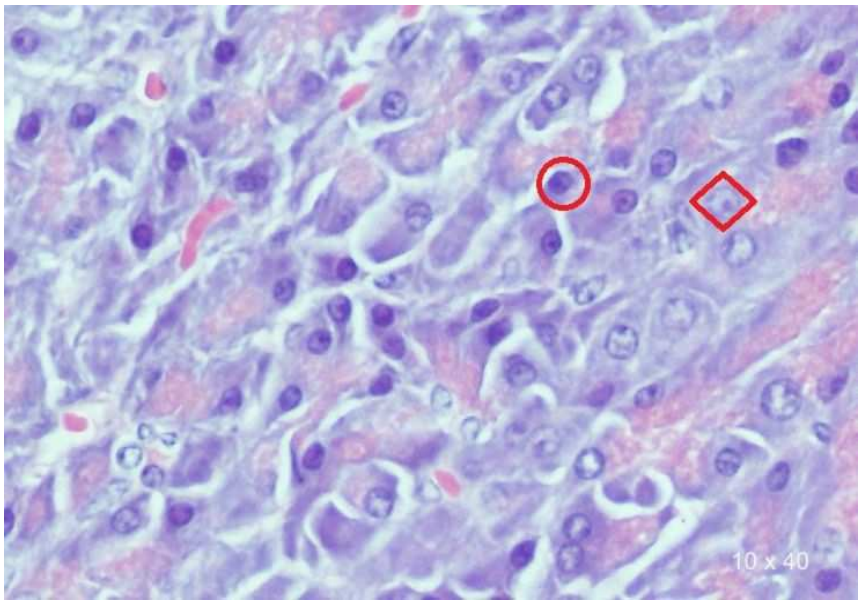
Gambar 11. Foto Histologi Pankreas (Zerumbon 13-OH 1,5 µg/kg BB)



Gambar 12. Foto Histologi Pankreas (Zerumbon 13-OH 2 µg/kg BB)



Gambar 13. Foto Histologi Pankreas (Gemcitabine®)



Gambar 14. Foto Histologi Pankreas (Kontrol Negatif)

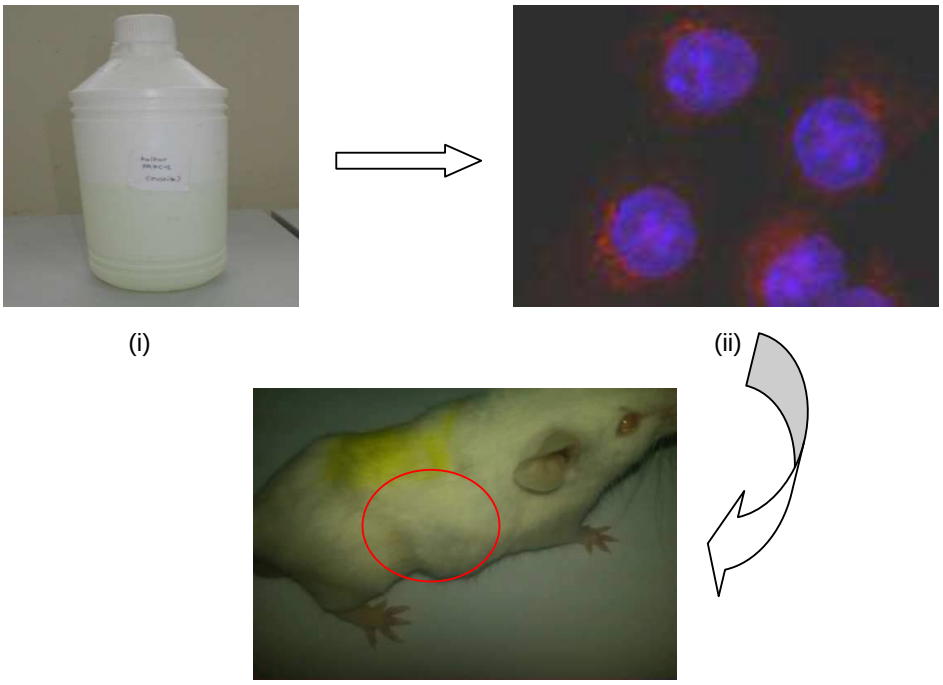
Keterangan gambar :

: Sel Normal

: Sel Nekrotik

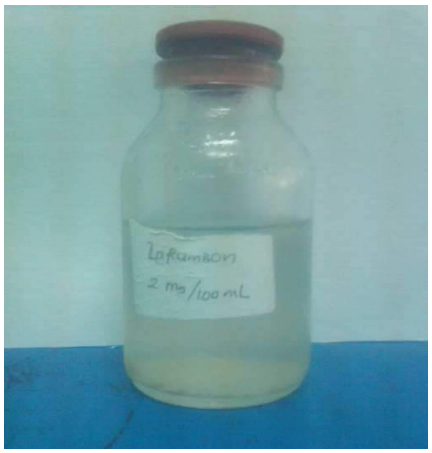
LAMPIRAN V

FOTO PENELITIAN



(i) (ii) (iii)

Gambar 15. (i) Kultur sel PANC1, (ii) Sel PANC1
(iii) Hewan coba yang telah megalami tumor.



Gambar 16. Zerumbon 13-OH