

## DAFTAR PUSTAKA

1. Wijaksana Evan IK. Periodontal Chart dan Periodontal Risk Assessment Sebagai Bahan Evaluasi dan Edukasi Pasien dengan Penyakit Periodontal. *J Kesehat Gigi*. 2019;6(3):19–25.
2. Passarelli PC, Pagnoni S, Piccirillo GB, Desantis V, Benegiamo M, Liguori A, et al. Reasons for tooth extractions and related risk factors in adult patients: A cohort study. *Int J Environ Res Public Health*. 2020;17(7).
3. Araújo MG, Silva CO, Misawa M, Sukekava F. Alveolar socket healing: What can we learn? *Periodontol 2000*. 2015;68(1):122–34.
4. Chappuis V, Araújo MG, Buser D. Clinical relevance of dimensional bone and soft tissue alterations post-extraction in esthetic sites. *Periodontol 2000*. 2017;73(1):73–83.
5. Hansson S, Halldin A. Alveolar ridge resorption after tooth extraction: A consequence of a fundamental principle of bone physiology. *J Dent Biomech*. 2012;3(1):1–8.
6. Landsberg C, Bender O, Weinreb M, Wigler R, Chackartchi T, Weinberg E, et al. Postextraction ridge width alterations following socket seal surgery—A retrospective study. *Appl Sci*. 2021;11(1):1–9.
7. Lin HK, Pan YH, Salamanca E, Lin Y Te, Chang WJ. Prevention of bone resorption by ha/β-tcp + collagen composite after tooth extraction: A case series. *Int J Environ Res Public Health*. 2019;16(23):1–11.
8. Juodzbaly G, Stumbras A, Goyushov S, Duruel O, Tözüm TF. Morphological Classification of Extraction Sockets and Clinical Decision Tree for Socket Preservation/Augmentation after Tooth Extraction: a Systematic Review. *J Oral Maxillofac Res*. 2019;10(3).
9. Velanita S, Ismardianita E, Pascawinata A. The effect of ant-plant (*Hydnophytum formicarum*) ethanol extract on collagen fibers for wound healing after tooth extraction in the guinea pig (*Cavia cobaya*). *Padjadjaran J Dent*. 2019;31(3):189.
10. Kattimani VS, Kondaka S, Lingamaneni KP. Hydroxyapatite—Past, Present, and Future in Bone Regeneration. *Bone Tissue Regen Insights*. 2016;7:BTRI.S36138.
11. Fiorellini JP, Kim D, Chang Y-C. Biofilm and Periodontal Microbiology. *Newman and Carranza's Clinical Periodontology*. 2018. 19 p.
12. Ramesh N, Ratnayake JTB, Moratti SC, Dias GJ. Effect of chitosan infiltration on hydroxyapatite scaffolds derived from New Zealand bovine cancellous bones for bone regeneration. *Int J Biol Macromol [Internet]*. 2020;160:1009–20. Available from: <https://doi.org/10.1016/j.ijbiomac.2020.05.269>
13. Boudemagh D, Venturini P, Fleutot S, Cleymand F. Elaboration of hydroxyapatite nanoparticles and chitosan/hydroxyapatite composites: a present status. Vol. 76, *Polymer Bulletin*. 2019. 2621–2653 p.
14. Nikpour MR, Rabiee SM, Jahanshahi M. Synthesis and characterization of hydroxyapatite/chitosan nanocomposite materials for medical engineering applications. *Compos Part B Eng [Internet]*. 2012;43(4):1881–6. Available from: <http://dx.doi.org/10.1016/j.compositesb.2012.01.056>
15. Tajrin A. Penyembuhan luka jaringan keras pascatrauma. *Makassar Dent J*. 2018;1(1):23.

16. Gonzalez ACDO, Andrade ZDA, Costa TF, Medrado ARAP. Wound healing - A literature review. *An Bras Dermatol*. 2016;91(5):614–20.
17. Bonewald LF. Osteocytes as dynamic multifunctional cells. *Ann N Y Acad Sci*. 2007;1116:281–90.
18. Dallas SL, Prideaux M, Bonewald LF. The osteocyte: An endocrine cell . . . and more. *Endocr Rev*. 2013;34(5):658–90.
19. Yan Z, Zhu S, Tian X, Ye Z, Zhai D, Zhu Z, et al. Metformin protects bone mass in ultra-high-molecular-weight polyethylene particle-induced osteolysis by regulating osteocyte secretion. *J Bone Miner Metab* [Internet]. 2019;37(3):399–410. Available from: <https://doi.org/10.1007/s00774-018-0939-7>
20. Soukas AA, Hao H, Wu L. Metformin as Anti-Aging Therapy: Is It for Everyone? *Trends Endocrinol Metab* [Internet]. 2019;30(10):745–55. Available from: <https://doi.org/10.1016/j.tem.2019.07.015>
21. Barzilai N, Crandall JP, Kritchevsky SB, Espeland MA. Metformin as a Tool to Target Aging. *Cell Metab* [Internet]. 2016;23(6):1060–5. Available from: <http://dx.doi.org/10.1016/j.cmet.2016.05.011>
22. Bai B, Chen H. Metformin: A Novel Weapon Against Inflammation. *Front Pharmacol*. 2021;12(January):1–12.
23. Saini N, Yang X. Metformin as an anti-cancer agent: Actions and mechanisms targeting cancer stem cells. *Acta Biochim Biophys Sin (Shanghai)*. 2018;50(2):133–43.
24. Matica MA, Aachmann FL, Tøndervik A, Sletta H, Ostafe V. Chitosan as a wound dressing starting material: Antimicrobial properties and mode of action. *Int J Mol Sci*. 2019;20(23):1–34.
25. John AV, Abraham G, Alias A. Two-visit CAD/CAM milled dentures in the rehabilitation of edentulous arches: A case series. *J Indian Prosthodont Soc*. 2019;19(1):88–92.
26. Gomes P de S, Daugela P, Poskevicius L, Mariano L, Fernandes MH. Molecular and Cellular Aspects of Socket Healing in the Absence and Presence of Graft Materials and Autologous Platelet Concentrates: a Focused Review. *J Oral Maxillofac Res*. 2019;10(3):1–18.
27. Jayaprakash R. A Review of Healing Potential of *Moringa olifera* Leaves in Wound. *Int J Pharm Sci Rev Res*. 2017;43(12):42–8.
28. Cohen Edward S. *Cosmetic and Reconstructive Periodontal Surgery*. 3rd ed. New York: BD Decker Inc Hamilton; 2007. 447 p.
29. Lafuente-Gracia L, Borgiani E, Nasello G, Geris L. Towards in silico Models of the Inflammatory Response in Bone Fracture Healing. *Front Bioeng Biotechnol*. 2021;9(September):1–22.
30. Aprilianti NA, Rahmadhani D, Rizqianti Y, Ridwan RD, Ramadhani NF, Nugraha AP. Periodontal ligament stem cells, solcoseryl pasta incorporated nano-hydroxyapatite silica gel scaffold for bone defect regeneration in chronic periodontitis: A review. *Biochem Cell Arch*. 2020;20:3101–6.
31. Loi F, Córdova LA, Pajarinen J, Lin T hua, Yao Z, Goodman SB. Inflammation, fracture and bone repair. *Bone*. 2016;86:119–30.
32. Lu LY, Loi F, Nathan K, Lin TH, Pajarinen J, Gibon E, et al. Pro-inflammatory M1 macrophages promote Osteogenesis by mesenchymal stem cells via the COX-2-prostaglandin E2 pathway. *J Orthop Res*. 2017;35(11):2378–85.
33. Bartold M, Gronthos S, Haynes D, Ivanovski S. Mesenchymal stem cells and biologic factors leading to bone formation. *J Clin Periodontol*. 2019;46(S21):12–32.

34. Lindhe J, Lang NP, Lang, N.P.; Lindhe J. *Clinical Periodontology and Implant Dentistry*. 6th ed. Lindhe J, Lang NP, editors. Vol. 121, *Clinical Periodontology and Implant Dentistry*. New Jersey: wiley blackwell; 2015. 796–800 p.
35. Kirpichnikov D, McFarlane SI, Sowers JR. Metformin: An update. *Ann Intern Med*. 2002;137(1):25–33.
36. Bonewald LF. The amazing osteocyte. *J Bone Miner Res*. 2011;26(2):229–38.
37. Franz-Odenaal TA, Hall BK, Witten PE. Buried alive: How osteoblasts become osteocytes. *Dev Dyn*. 2006;235(1):176–90.
38. Mani V, Wasalathanthri D. 1,2,3\* 1. 2009;585:2009.
39. Zhang K, Barragan-Adjemian C, Ye L, Kotha S, Dallas M, Lu Y, et al. E11/gp38 Selective Expression in Osteocytes: Regulation by Mechanical Strain and Role in Dendrite Elongation. *Mol Cell Biol*. 2006;26(12):4539–52.
40. Rochefort GY, Pallu S, Benhamou CL. Osteocyte: The unrecognized side of bone tissue. *Osteoporos Int*. 2010;21(9):1457–69.
41. Palumbo C, Ferretti M, Marotti G. Osteocyte Dendrogenesis in Static and Dynamic Bone Formation: An Ultrastructural Study. *Anat Rec - Part A Discov Mol Cell Evol Biol*. 2004;278(1):474–80.
42. Cao W, Helder MN, Bravenboer N, Wu G, Jin J, ten Bruggenkate CM, et al. Is There a Governing Role of Osteocytes in Bone Tissue Regeneration? *Curr Osteoporos Rep*. 2020;18(5):541–50.
43. Choy MHV, Wong RMY, Chow SKH, Li MC, Chim YN, Li TK, et al. How much do we know about the role of osteocytes in different phases of fracture healing? A systematic review. *J Orthop Transl*. 2020;21(xxxx):111–21.
44. Li M, Amizuka N, Oda K, Tokunaga K, Ito T, Takeuchi K, et al. Histochemical evidence of the initial chondrogenesis and osteogenesis in the periosteum of a rib fractured model: Implications of osteocyte involvement in periosteal chondrogenesis. *Microsc Res Tech*. 2004;64(4):330–42.
45. Dishowitz MI, Mutyaba PL, Takacs JD, Barr AM, Engiles JB, Ahn J, et al. Systemic Inhibition of Canonical Notch Signaling Results in Sustained Callus Inflammation and Alters Multiple Phases of Fracture Healing. *PLoS One*. 2013;8(7):1–14.
46. Neagu TP, Țigliș M, Popp CG, Jecan CR. Histological assessment of fracture healing after reduction of the rat femur using two different osteosynthesis methods. *Rom J Morphol Embryol*. 2016;57(3):1051–6.
47. Jung RE, Sapata VM, Hämmerle CHF, Wu H, Hu XL, Lin Y. Combined use of xenogeneic bone substitute material covered with a native bilayer collagen membrane for alveolar ridge preservation: A randomized controlled clinical trial. *Clin Oral Implants Res*. 2018;29(5):522–9.
48. Avila-Ortiz G, Gubler M, Romero-Bustillos M, Nicholas CL, Zimmerman MB, Barwacz CA. Efficacy of Alveolar Ridge Preservation: A Randomized Controlled Trial. *J Dent Res*. 2020;99(4):402–9.
49. Adel-Khattab D, Afifi NS, Abu el Sadat SM, Aboul-Fotouh MN, Tarek K, Horowitz RA. Bone regeneration and graft material resorption in extraction sockets grafted with bioactive silica-calcium phosphate composite (SCPC) versus non-grafted sockets: clinical, radiographic, and histological findings. *J Periodontal Implant Sci*. 2020;50(6):1–17.
50. Kim YK, Ku JK. Extraction socket preservation. *J Korean Assoc Oral Maxillofac Surg*. 2020;46(6):435–9.
51. Pranskunas M, Galindo-Moreno P, Padiál-Molina M. Extraction Socket Preservation Using Growth Factors and Stem Cells: a Systematic Review. *J Oral*

- Maxillofac Res. 2019;10(3):1–11.
52. Formiga M de C, Dayube URC, Chiapetti CK, Figueiredo D de R, Shibli JA. Socket preservation using a (dense) PTFE barrier with or without xenograft material: A randomized clinical trial. *Materials (Basel)*. 2019;12(18).
  53. Miron RJ, Moraschini V, Fujioka-Kobayashi M, Zhang Y, Kawase T, Cosgarea R, et al. Use of platelet-rich fibrin for the treatment of periodontal intrabony defects: a systematic review and meta-analysis. *Clin Oral Investig*. 2021 May;25(5):2461–78.
  54. Zhao R, Yang R, Cooper PR, Khurshid Z, Shavandi A, Ratnayake J. Bone grafts and substitutes in dentistry: A review of current trends and developments. *Molecules*. 2021;26(10):1–27.
  55. AlGhamdi AS, Shibly O, Ciancio SG. Osseous grafting part II: xenografts and alloplasts for periodontal regeneration--a literature review. *J Int Acad Periodontol*. 2010;12(2):39–44.
  56. Myron Spector. *Clinics in Plastic Surgery*. In: *Clinics in Plastic Surgery*. 1994. p. 437.
  57. Sculean A, Stavropoulos A, Windisch P, Keglevich T, Karring T, Gera I. Healing of human intrabony defects following regenerative periodontal therapy with a bovine-derived xenograft and guided tissue regeneration. *Clin Oral Investig*. 2004;8(2):70–4.
  58. Górski B, Jalowski S, Górski R, Zaremba M. Treatment of intrabony defects with modified perforated membranes in aggressive periodontitis: subtraction radiography outcomes, prognostic variables, and patient morbidity. *Clin Oral Investig*. 2019;23(7):3005–20.
  59. Baldini N, De Sanctis M, Ferrari M. Deproteinized bovine bone in periodontal and implant surgery. *Dent Mater [Internet]*. 2011;27(1):61–70. Available from: <http://dx.doi.org/10.1016/j.dental.2010.10.017>
  60. De Bruyckere T, Eghbali A, Younes F, Cleymaet R, Jacquet W, De Bruyn H, et al. A 5-year prospective study on regenerative periodontal therapy of infrabony defects using minimally invasive surgery and a collagen-enriched bovine-derived xenograft. *Clin Oral Investig*. 2018;22(3):1235–42.
  61. Sundaram G, Ramakrishnan T, Parthasarathy H, Raja M, Raj S. disease : A cross - link of sorts ! 2018;(May):113–8.
  62. Chiapasco M, Tommasato G, Palombo D, Del Fabbro M. A retrospective 10-year mean follow-up of implants placed in ridges grafted using autogenous mandibular blocks covered with bovine bone mineral and collagen membrane. *Clin Oral Implants Res*. 2020;31(4):328–40.
  63. Sheikh Z, Hamdan N, Ikeda Y, Grynypas M, Ganss B, Glogauer M. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: A review. *Biomater Res*. 2017;21(1):1–20.
  64. Orsini G, Scarano A, Piattelli M, Piccirilli M, Caputi S, Piattelli A. Histologic and Ultrastructural Analysis of Regenerated Bone in Maxillary Sinus Augmentation Using a Porcine Bone-Derived Biomaterial. *J Periodontol*. 2006;77(12):1984–90.
  65. Scarano A, Piattelli A, Assenza B, Quaranta A, Perrotti V, Piattelli M, et al. Porcine bone used in sinus augmentation procedures: A 5-year retrospective clinical evaluation. *J Oral Maxillofac Surg [Internet]*. 2010;68(8):1869–73. Available from: <http://dx.doi.org/10.1016/j.joms.2009.09.015>
  66. Lee D, Park J. v o i i s r n o l a v o i i s n o l a v o i i s r n o l a. 2023;53(1):1–15.
  67. Guarnieri R, Stefanelli L, De Angelis F, Mencio F, Pompa G, Di Carlo S. Extraction Socket Preservation Using Porcine-Derived Collagen Membrane Alone

- or Associated with Porcine-Derived Bone. Clinical Results of Randomized Controlled Study. *J Oral Maxillofac Res.* 2017;8(3):1–9.
68. Balaji V, Manikandan D, Ramsundar A. Bone grafts in periodontics. *Matrix Sci Medica.* 2020;4(3):57.
  69. Damien E, Revell PA. Coralline hydroxyapatite bone graft substitute: A review of experimental studies and biomedical applications. *J Appl Biomater Biomech* [Internet]. 2004;2(2):65–73. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20803439>
  70. Sheikh Z, Sima C, Glogauer M. Bone replacement materials and techniques used for achieving vertical alveolar bone augmentation. *Materials (Basel).* 2015;8(6):2953–93.
  71. Gokul K, Arunachalam D, Balasundaram S, Balasundaram A. Validation of Bone Therapy-a Review Grafts in. *Int J Cur Res Rev.* 2014;06(14):7–17.
  72. Puvaneswary S, Balaji Raghavendran HR, Syuhada Ibrahim NS, Murali MR, Mahmood Merican A, Kamarul T. A comparative study on morphochemical properties and osteogenic cell differentiation within bone graft and coral graft culture systems. *Int J Med Sci.* 2013;10(12):1608–14.
  73. Matuda Y, Okamura T, Tabata H, Yasui K, Tatsumura M, Kobayashi N, et al. Periodontal regeneration using cultured coral scaffolds in class ii furcation defects in dogs. *J Hard Tissue Biol.* 2019;28(4):329–34.
  74. Mahanani ES, Bachtiar I, Ana ID. The porosity and human gingival cells attachment of synthetic coral scaffold for bone regeneration. *Key Eng Mater.* 2020;840 KEM(March 2021):305–10.
  75. Hermann LS, Schersten B, Bitzen P-O, Kjellstrom T, Lindgarde F, Arne M. Therapeutic Comparison. 1994;17(10):1100–9.
  76. Allen, DP, Eberhart C, Williams W. 5726. *Am Math Mon.* 1971;78(4):412.
  77. Pasquali R, Gambineri A, Biscotti D, Vicennati V, Gagliardi L, Colitta D, et al. Effect of long-term treatment with metformin added to hypocaloric diet on body composition, fat distribution, and androgen and insulin levels in abdominally obese women with and without the polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2000;85(8):2767–74.
  78. Yerevanian A, Soukas AA. Metformin: Mechanisms in Human Obesity and Weight Loss. *Curr Obes Rep.* 2019;8(2):156–64.
  79. McCreight LJ, Bailey CJ, Pearson ER. Metformin and the gastrointestinal tract. *Diabetologia.* 2016;59(3):426–35.
  80. Agius L, Ford BE, Chachra SS. The metformin mechanism on gluconeogenesis and AMPK activation: The metabolite perspective. *Int J Mol Sci.* 2020;21(9).
  81. Coughlan KA, Valentine RJ, Ruderman NB, Saha AK, Inzucchi SE, Dennis T, et al. Role of AMP-activated protein kinase in mechanism of metformin action. *J Biol Chem* [Internet]. 2005;13(1):1–10. Available from: <http://www.who.int/about/licensing/><http://www.jci.org/cgi/content/abstract/108/8/1167><http://dx.doi.org/10.1016/j.cell.2011.07.039><http://dx.doi.org/10.1038/ncomms4017><http://dx.doi.org/10.1016/j.molcel.2013.01.035><http://www.ncbi.nlm.nih.gov/p>
  82. Joijcjt F, Hmvdpofphoftjt I, Njdf JO, Pg J, Wjb Q, Jo BE, et al. Fofshz Tubuf. *Changes.* 2010;120(7):2355–69.
  83. Kristófi R, Eriksson JW. Metformin as an anti-inflammatory agent: A short review. *J Endocrinol.* 2021;251(2):R11–22.
  84. Araújo AA de, Pereira A de SBF, Medeiros CACX de, Brito GA de C, Leitão RF de C, Araújo L de S, et al. Effects of metformin on inflammation, oxidative stress,

- and bone loss in a rat model of periodontitis. *PLoS One*. 2017;12(8):e0183506.
85. Velanita S, Ismardianita E, Pascawinata A. The effect of ant-plant (*Hydnophytum formicarum*) ethanol extract on collagen fibers for wound healing after tooth extraction in the guinea pig (*Cavia cobaya*). *Padjadjaran J Dent*. 2019;31(3):189..
  86. Cortizo AM, Sedlinsky C, McCarthy AD, Blanco A, Schurman L. Osteogenic actions of the anti-diabetic drug metformin on osteoblasts in culture. *Eur J Pharmacol*. 2006;536(1–2):38–46.
  87. Shah M, Kola B, Bataveljic A, Arnett TR, Viollet B, Saxon L, et al. AMP-activated protein kinase (AMPK) activation regulates in vitro bone formation and bone mass. *Bone* [Internet]. 2010;47(2):309–19. Available from: <http://dx.doi.org/10.1016/j.bone.2010.04.596>
  88. Mohapatra A, Parikh R, Gohel M. Formulation, development and evaluation of patient friendly dosage forms of metformin, Part-II: Oral soft gel. *Asian J Pharm*. 2008;2(3):172.
  89. Ebrahimi L, Farzin A, Ghasemi Y, Alizadeh A, Goodarzi A, Basiri A, et al. Metformin-Loaded PCL/PVA Fibrous Scaffold Preseeded with Human Endometrial Stem Cells for Effective Guided Bone Regeneration Membranes. *ACS Biomater Sci Eng*. 2021;7(1):222–31.
  90. Zhu M, Zhao Z, Xu H, Dai Z, Yu K, Xiao L, et al. Effects of Metformin Delivery via Biomaterials on Bone and Dental Tissue Engineering. *Int J Mol Sci*. 2022;23(24).
  91. Hu Z, Qiu W, Yu Y, Wu X, Fang F, Zhu X, et al. Identification and Characterization of a Novel Long Noncoding RNA that Regulates Osteogenesis in Diet-Induced Obesity Mice. *Front Cell Dev Biol*. 2022;10(April):1–13.
  92. Shahrezaee M, Salehi M, Keshtkari S, Oryan A, Kamali A, Shekarchi B. In vitro and in vivo investigation of PLA/PCL scaffold coated with metformin-loaded gelatin nanocarriers in regeneration of critical-sized bone defects. *Nanomedicine Nanotechnology, Biol Med* [Internet]. 2018;14(7):2061–73. Available from: <https://doi.org/10.1016/j.nano.2018.06.007>
  93. Ebrahimi L, Farzin A, Ghasemi Y, Alizadeh A, Goodarzi A, Basiri A, et al. Metformin-Loaded PCL/PVA Fibrous Scaffold Preseeded with Human Endometrial Stem Cells for Effective Guided Bone Regeneration Membranes. *ACS Biomater Sci Eng*. 2021;7(1):222–31.
  94. Shao Z, Liu J, Schneider A, Gao X, Ren K, Weir MD, et al. Human periodontal ligament stem cell seeding on calcium phosphate cement scaffold delivering metformin for bone tissue engineering. *J Dent* [Internet]. 2019;91:103220. Available from: <https://doi.org/10.1016/j.jdent.2019.103220>
  95. Zhang R, Liang Q, Kang W, Ge S. Metformin facilitates the proliferation, migration, and osteogenic differentiation of periodontal ligament stem cells in vitro. *Cell Biol Int*. 2020;44(1):70–9.

## LAMPIRAN LEMBAR ETIK



KEMENTERIAN RISET, TEKNOLOGI DAN PENDIDIKAN TINGGI  
UNIVERSITAS HASANUDDIN  
FAKULTAS KEDOKTERAN GIGI  
RUMAH SAKIT GIGI DAN MULUT  
KOMITE ETIK PENELITIAN KESEHATAN  
Sekretariat : Lantai 2, Gedung Lama RSGM Unhas  
JL. Kondea No. 5 Makassar



Contact Person: drg. Muhammad Ikbal, Sp.Prof/Nur Andah AR TELP. 081342971011/08114919191

### REKOMENDASI PERSETUJUAN ETIK Nomor: 0057/PL.09/KEPK FK-G-RSGM UNHAS/2023

Tanggal: 10 April 2023

Dengan ini menyatakan bahwa protokol dan dokumen yang berhubungan dengan protokol berikut ini telah mendapatkan persetujuan etik:

No. Protokol	UH 17120794	No Protokol Sponsor	
Peneliti Utama	drg. Patrisia Seroja Ningrum	Sponsor	Pribadi
Judul Peneliti	Potensi Penggunaan Gel Metformin 1% dan Xenografi terhadap Jumlah Osteosit pada tindakan Soket Preservation		
No. Versi Protokol	1	Tanggal Versi	31 Maret 2023
No. Versi Protokol		Tanggal Versi	
Tempat Penelitian	1. Laboratorium Biofarmaka Fakultas Farmasi Universitas Hasanuddin 2. Klinik Hewan Doc pet 3. Laboratorium PA RSP Universitas Hasanuddin 4. Laboratorium Biokimia-Biomolekuler Fakultas Kedokteran Universitas Brawijaya		
Dokumen Lain			
Jenis Review	<input type="checkbox"/> Exempted <input checked="" type="checkbox"/> Expedited <input type="checkbox"/> Fullboard	Masa Berlaku 10 April 2023-10 April 2024	Frekuensi Review Lanjutan
Ketua Komisi Etik Penelitian	Nama: Dr. drg. Marhamah, M.Kes	Tanda Tangan 	Tanggal
Sekretaris Komisi Etik Penelitian	Nama: drg. Muhammad Ikbal, Sp.Prof	Tanda Tangan 	Tanggal

**Kewajiban peneliti utama:**

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum diimplementasikan
- Menyerahkan laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan lapor 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 aturan yang berlak

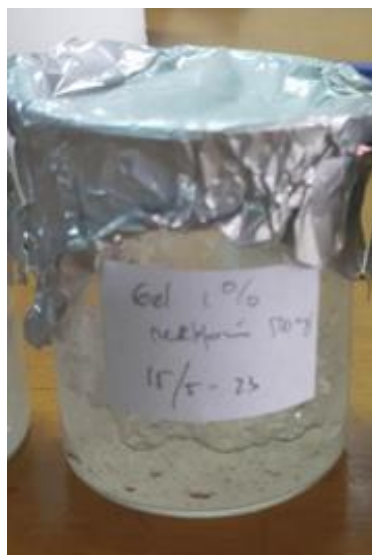


Dipindai dengan CamScanner

**LAMPIRAN**  
**FOTO-FOTO PROSES PENELITIAN**

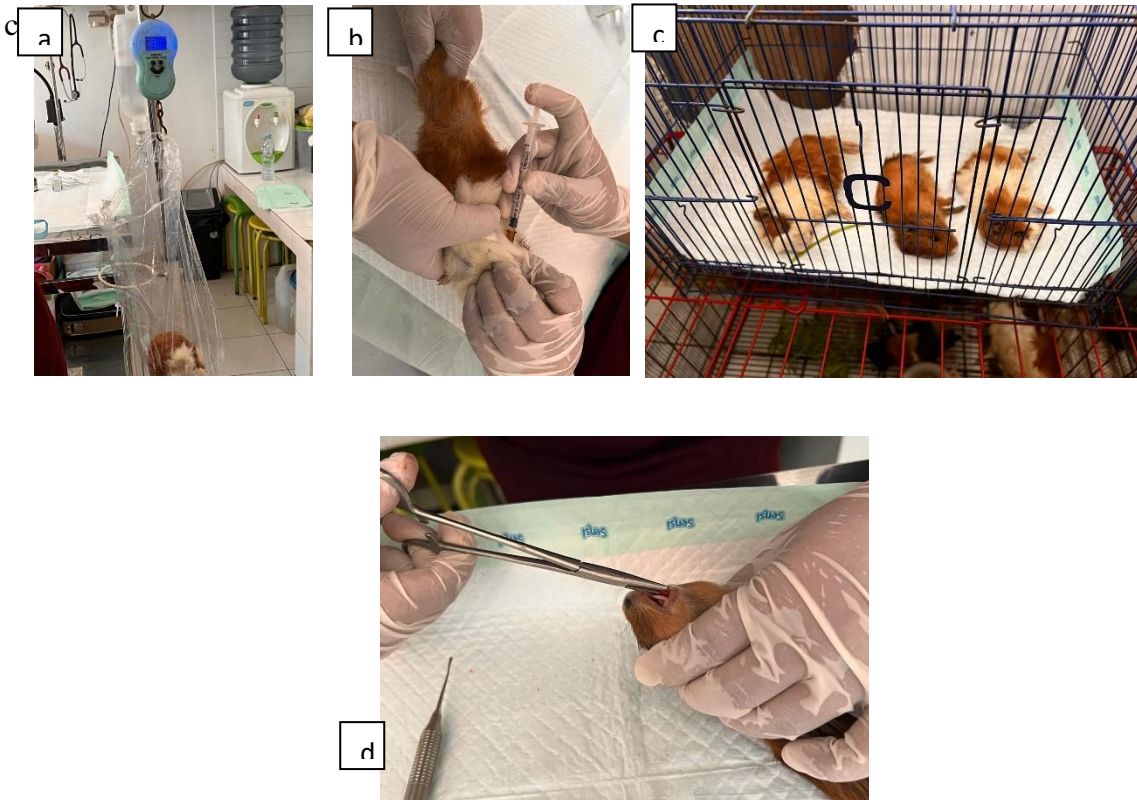


**Gambar 9.** Proses pembuatan Gel Metformin 1% (6 Juli 2023).(a).Bubuk metformin murni sebanyak 2 gr (b).Bahan lain : manitol, citric acid, methyl parabean, sodium citrate, sucrose, prophyll parabean, gellan gum (c). Proses pemanasan semua bahan sesuai takaran hingga mencapai konsistensi yang diinginkan

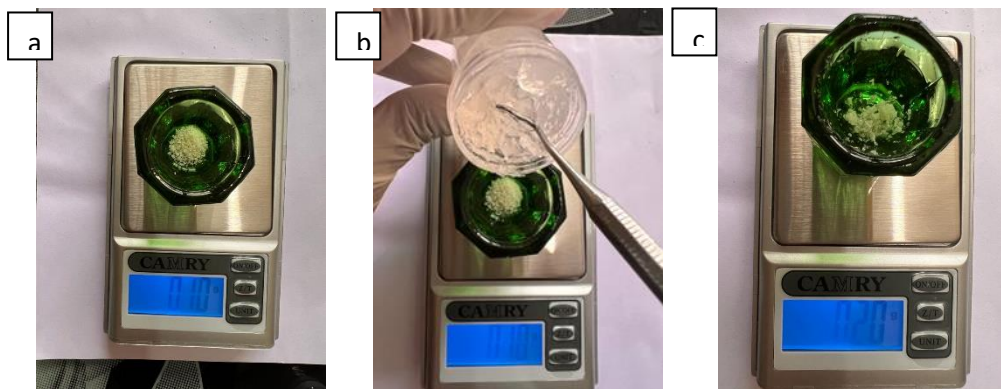


**Gambar 10.** Gel Metformin 1%

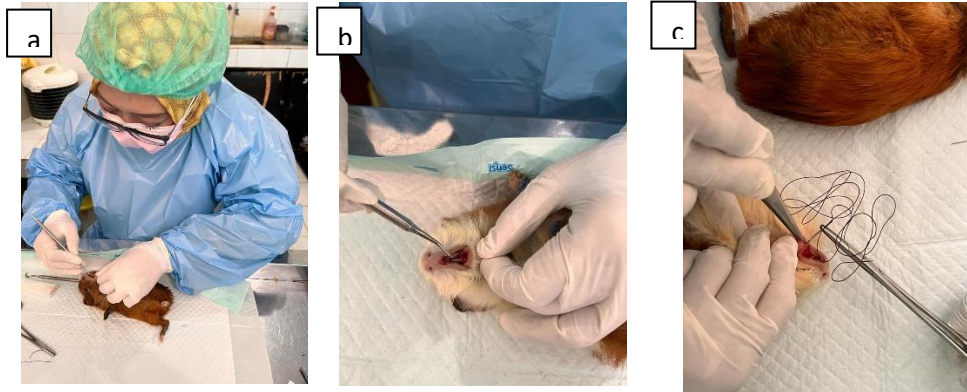




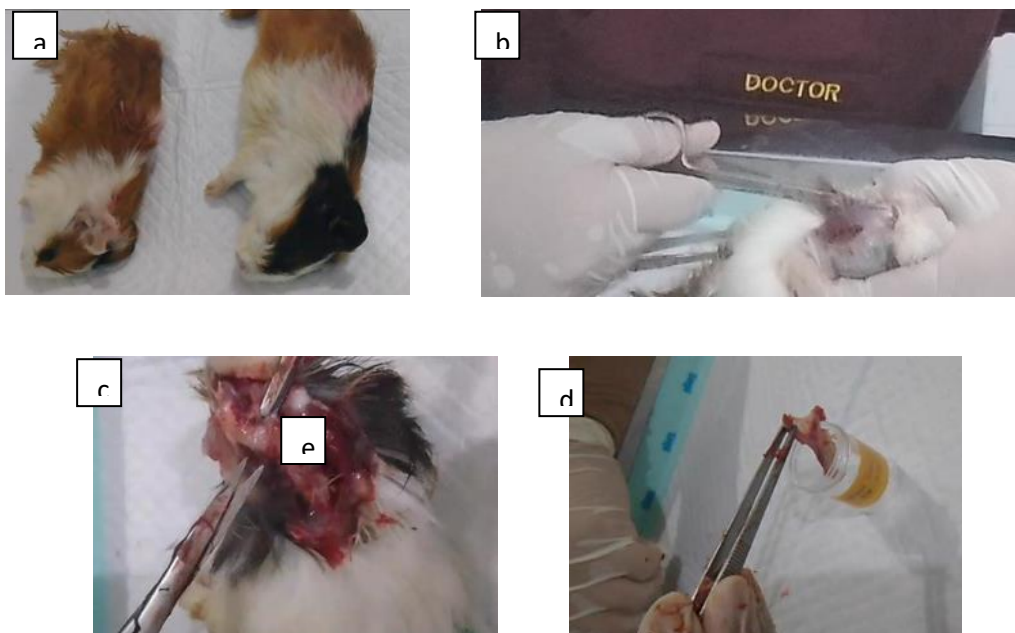
**Gambar 11.** Setelah marmut diadaptasikan selama 7 hari (30 Mei 2023), marmut dibagi menjadi 3 kelompok yaitu kelompok I (soket diisi dengan kombinasi gel metformin 1% dan xenograft), kelompok II (soket diisi xenograft/kontrol positif), dan kelompok III tanpa perlakuan (kontrol negatif). (a) Marmut ditimbang sesuai berat pada kriteria inklusi 250-300 gr (b) Anastesi dengan injeksi ketamin (c) Marmut yang sudah dianastesi (d) Pencabutan gigi insivus mandibula marmut

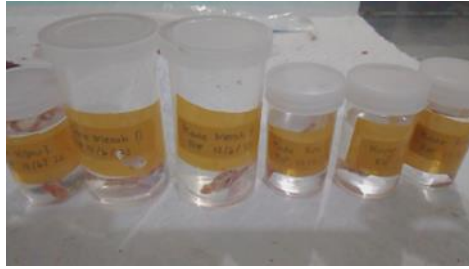


**Gambar 12.** Pencampuran gel metformin 1% dan xenograft dengan perbandingan 1:1. (a) Xenograft 0.10 gr (b) Gel metformin 1% 0.10 gr. (c) Kombinasi gel metformin 1% dan xenograft 0.20 gr

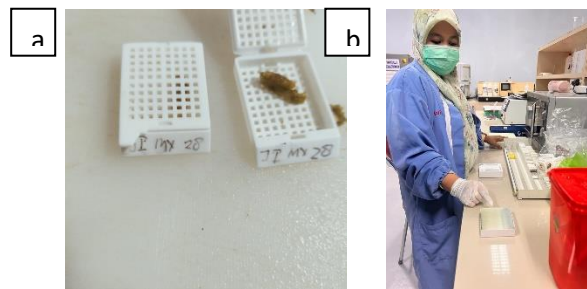


**Gambar13.** (a) Proses memasukkan kombinasi gel meformin 1% dan xenograft kedalam socket bekas pencabutan gigi marmut. (b) Memasukkan bahan uji dengan bantuan excavator. (c) Penjahitan socket yang sudah diisi bahan uji dengan menggunakan benang black silk





**Gambar 14.** (a-e) Setelah pencabutan gigi insisivus rahang bawah dan diberi perlakuan, marmut dikorbankan pada hari ke 7, 14, dan 28 untuk pengambilan jaringan pada rahang mandibula dan difiksasi menggunakan larutan buffer formalin 10% sebagai sampel penelitian



**Gambar 15.** (a) Sampel dibawa ke lab Patologi Anatomi untuk dilunakkan dan dibuat sampel preparatnya (12 juli 2023). (b) Slide preparat yang sudah siap kirim ke laboratorium Biokimia-Biomolekuler Universitas Brawijaya untuk dilakukan pemeriksaan histologis (28 juli 2023)

## Lampiran Output SPSS.24

### Tests of Normality

Kelompok	Kolmogorov-Smirnov <sup>a</sup>			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Osteosit	.187	9	.200 <sup>*</sup>	.959	9	.789
Perlakuan	.187	9	.200 <sup>*</sup>	.937	9	.547
Kontrol Positif	.161	9	.200 <sup>*</sup>	.971	9	.907
Kontrol Negatif						

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

a. Lilliefors Significance Correction

## T-Test (hari ke 7)

### Group Statistics

Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit				
Perlakuan	3	11.0000	2.00000	1.15470
Kontrol Positif	3	7.0000	1.00000	.57735

### Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means			95% Confidence Interval of the Difference			
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.800	.422	3.098	4	.036	4.00000	1.29099	.41562	7.58438
	Equal variances not assumed			3.098	2.941	.055	4.00000	1.29099	-.15540	8.15540

### Group Statistics

Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit				
Perlakuan	3	11.0000	2.00000	1.15470
Kontrol Negatif	3	3.3333	1.52753	.88192

### Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.727	.442	3.479	4	.025	3.66667	1.05409	.74004	6.59330
	Equal variances not assumed			3.479	3.448	.032	3.66667	1.05409	.54578	6.78755

### Group Statistics

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit	Kontrol Positif	3	7.0000	1.00000	.57735
	Kontrol Negatif	3	3.3333	1.52753	.88192

### Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.727	.442	3.479	4	.025	3.66667	1.05409	.74004	6.59330
	Equal variances not assumed			3.479	3.448	.032	3.66667	1.05409	.54578	6.78755

## Oneway

### Descriptives

Osteosit

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Perlakuan	3	11.0000	2.00000	1.15470	6.0317	15.9683	9.00	13.00
Kontrol Positif	3	7.0000	1.00000	.57735	4.5159	9.4841	6.00	8.00
Kontrol Negatif	3	3.3333	1.52753	.88192	-.4612	7.1279	2.00	5.00
Total	9	7.1111	3.58624	1.19541	4.3545	9.8677	2.00	13.00

## ANOVA

Osteosit

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	88.222	2	44.111	18.045	.003
Within Groups	14.667	6	2.444		
Total	102.889	8			

## Multiple Comparisons

Dependent Variable: Osteosit

LSD

(I) Kelompok	(J) Kelompok	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Perlakuan	Kontrol Positif	4.00000*	1.27657	.020	.8763	7.1237
	Kontrol Negatif	7.66667*	1.27657	.001	4.5430	10.7903
Kontrol Positif	Perlakuan	-4.00000*	1.27657	.020	-7.1237	-.8763
	Kontrol Negatif	3.66667*	1.27657	.028	.5430	6.7903
Kontrol Negatif	Perlakuan	-7.66667*	1.27657	.001	-10.7903	-4.5430
	Kontrol Positif	-3.66667*	1.27657	.028	-6.7903	-.5430

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

HARI KE-14

## Group Statistics

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit	Perlakuan	3	12.6667	1.52753	.88192
	Kontrol Positif	3	8.0000	1.00000	.57735

**Independent Samples Test**

		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.727	.442	4.427	4	.011	4.66667	1.05409	1.74004	7.59330
	Equal variances not assumed			4.427	3.448	.016	4.66667	1.05409	1.54578	7.78755

**Group Statistics**

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit	Perlakuan	3	12.6667	1.52753	.88192
	Kontrol Negatif	3	5.0000	1.00000	.57735

**Independent Samples Test**

		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.727	.442	7.273	4	.002	7.66667	1.05409	4.74004	10.59330
	Equal variances not assumed			7.273	3.448	.003	7.66667	1.05409	4.54578	10.78755

**Group Statistics**

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit	Kontrol Positif	3	8.0000	1.00000	.57735
	Kontrol Negatif	3	5.0000	1.00000	.57735

**Independent Samples Test**

		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.000	1.000	3.674	4	.021	3.00000	.81650	.73304	5.26696
	Equal variances not assumed			3.674	4.000	.021	3.00000	.81650	.73304	5.26696

### Descriptives

Osteosit

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Perlakuan	3	12.6667	1.52753	.88192	8.8721	16.4612	11.00	14.00
Kontrol Positif	3	8.0000	1.00000	.57735	5.5159	10.4841	7.00	9.00
Kontrol Negatif	3	5.0000	1.00000	.57735	2.5159	7.4841	4.00	6.00
Total	9	8.5556	3.50397	1.16799	5.8622	11.2489	4.00	14.00

### ANOVA

Osteosit

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	89.556	2	44.778	31.000	.001
Within Groups	8.667	6	1.444		
Total	98.222	8			

### Multiple Comparisons

Dependent Variable: Osteosit

LSD

(I) Kelompok	(J) Kelompok	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Perlakuan	Kontrol Positif	4.66667*	.98131	.003	2.2655	7.0678
	Kontrol Negatif	7.66667*	.98131	.000	5.2655	10.0678
Kontrol Positif	Perlakuan	-4.66667*	.98131	.003	-7.0678	-2.2655
	Kontrol Negatif	3.00000*	.98131	.022	.5988	5.4012
Kontrol Negatif	Perlakuan	-7.66667*	.98131	.000	-10.0678	-5.2655
	Kontrol Positif	-3.00000*	.98131	.022	-5.4012	-.5988

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



**Group Statistics**

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit	Perlakuan	3	15.0000	1.00000	.57735
	Kontrol Positif	3	10.6667	1.52753	.88192

**Independent Samples Test**

		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.727	.442	4.111	4	.015	4.33333	1.05409	1.40670	7.25996
	Equal variances not assumed			4.111	3.448	.020	4.33333	1.05409	1.21245	7.45422

**Group Statistics**

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit	Perlakuan	3	15.0000	1.00000	.57735
	Kontrol Negatif	3	7.6667	1.52753	.88192

**Independent Samples Test**

		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Osteosit	Equal variances assumed	.727	.442	6.957	4	.002	7.33333	1.05409	4.40670	10.25996
	Equal variances not assumed			6.957	3.448	.004	7.33333	1.05409	4.21245	10.45422

### Group Statistics

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Osteosit	Kontrol Positif	3	10.6667	1.52753	.88192
	Kontrol Negatif	3	7.6667	1.52753	.88192

### Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Osteosit	Equal variances assumed	.000	1.000	2.405	4	.074	3.00000	1.24722	-.46284	6.46284
	Equal variances not assumed			2.405	4.000	.074	3.00000	1.24722	-.46284	6.46284

### Descriptives

Osteosit

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Perlakuan	3	15.0000	1.00000	.57735	12.5159	17.4841	14.00	16.00
Kontrol Positif	3	10.6667	1.52753	.88192	6.8721	14.4612	9.00	12.00
Kontrol Negatif	3	7.6667	1.52753	.88192	3.8721	11.4612	6.00	9.00
Total	9	11.1111	3.40751	1.13584	8.4919	13.7304	6.00	16.00

### ANOVA

Osteosit

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	81.556	2	40.778	21.588	.002
Within Groups	11.333	6	1.889		
Total	92.889	8			

### Multiple Comparisons

Dependent Variable: Osteosit

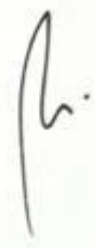

LSD

(I) Kelompok	(J) Kelompok	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Perlakuan	Kontrol Positif	4.33333 <sup>*</sup>	1.12217	.008	1.5875	7.0792
	Kontrol Negatif	7.33333 <sup>*</sup>	1.12217	.001	4.5875	10.0792
Kontrol Positif	Perlakuan	-4.33333 <sup>*</sup>	1.12217	.008	-7.0792	-1.5875
	Kontrol Negatif	3.00000 <sup>*</sup>	1.12217	.037	.2542	5.7458
Kontrol Negatif	Perlakuan	-7.33333 <sup>*</sup>	1.12217	.001	-10.0792	-4.5875
	Kontrol Positif	-3.00000 <sup>*</sup>	1.12217	.037	-5.7458	-.2542

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

## LEMBAR PERBAIKAN UJIAN SEMINAR HASIL PPDGS PERIODONSIA

**NAMA** : Patrisia Seroja Ningrum  
**NIM** : J035202004  
**TANGGAL SEMINAR** : 25 Oktober 2023  
**JUDUL** : Potensi Penggunaan Gel Metformin 1% dan Xenograft terhadap Jumlah Osteosit pada Tindakan *Socket Preservation*

NO	NAMA DOSEN PENGUJI/PEMBIMBING	KOREKSI TESIS	PARAF
1.	Dr. drg. Arni Irawaty Djais, Sp.Perio (K)	<p>1. Disarankan untuk memperbaiki letak penulisan pada keterangan gambar pada halaman 9  <b>Jawaban :</b>                      Telah dilakukan perbaikan letak penulisan pada keterangan gambar pada halaman 9</p> <p>2. Disarankan untuk tidak menggunakan kalimat dalam paragraf yang terlalu panjang pada halaman 10  <b>Jawaban :</b>                      Telah dilakukan perbaikan kalimat dalam paragraf pada halaman 10</p>	
2	Prof. Dr. drg. Hasanuddin Thahir, MS, Sp.Perio (K)	<p>1. Tujuan dan Simpulan harus sesuai  <b>Jawaban :</b>                      Telah dilakukan penyesuaian pada tujuan dan simpulan</p> <p>2. Penulisan Kesimpulan diubah menjadi Simpulan  <b>Jawaban :</b>                      Telah dilakukan perubahan pada penulisan Kesimpulan menjadi Simpulan</p>	
3.	Prof. Dr. drg. Sri Oktawati, Sp.Perio (K)	<p>1. Disarankan untuk tidak menggunakan kalimat dalam paragraf yang terlalu panjang pada halaman 12  <b>Jawaban :</b>                      Telah dilakukan perbaikan kalimat dalam paragraf pada halaman 12</p> <p>2. Koreksi penulisan hari penelitian dari hari ke 21 menjadi hari ke 28  <b>Jawaban :</b>                      Telah dilakukan koreksi penulisan hari penelitian dari hari ke 21 menjadi hari ke 28</p> <p>3. Dicantumkan satuan jumlah sel osteosit  <b>Jawaban :</b>                      Telah dilakukan pencantuman satuan jumlah sel osteosit</p>	