

DAFTAR PUSTAKA

- Bao-qiang, S., Yang, Z., Wei, Z., *et al.*, 2008. The influence of antiangiogenesis by gene transfection on expression of VEGF in hypertrophic scar. *Chin. J. Aesthetic Plast Surg.* www.cnki.com.cn
- Bayat, A., McGrouther, D.A., Ferguson, M.W. 2003. Skin Scarring. *BMJ*; 326: 88-92
- Bissek, A.Z., Tabah, E.N., Kouotou, E., Sini, V., Yepnjio, F.N., Nditanchou, R., *et al.* 2012. The Spectrum of Skin Diseases in a Rural Setting in Cameroon (Sub-Saharan Africa). *BMC Dermatology*; 1-9
- Bitzer, M., Opitz, H., Popp, J., Morgalla, M., Gruber, A., Heiss, E., Voigt, K. 1998. Angiogenesis and Brain Oedema in Intracranial Meningiomas: Influence of Vascular Endothelial Growth Factor. *Acta Neurochir (Wien)*. 140: 333- 340.
- Bosco, M.C., Puppo, M., Blengio, F., Fraone, T., Capello, P., Giovarelli, M., Varesio, L. Monocytes and dendritic cells in a hypoxic environment: Spotlights on chemotaxis and migration. *Immunobiology* 2008; 213: 733.
- Broughton, G., Janis, J.E., Attinger, C.E. 2006. Wound Healing: An Overview. *Plast Reconstr Surg*; 117: 1e-S-32e-S
- Burrows, N.P., Lovell, C.R. 2004. Keloid and Hypertrophic scars. In: Burns T, Breathach S, Cox n, Griffiths C., editors. *Rook's Textbook of Dermatology*. 7thEd. USA: Blackwell Publishing. p.54-56
- Butler, P.D., Longaker, M.T., Yang, G.P., 2008. Current progress in Keloid Research and Treatment. *J. Am Coll of Surg*; 206(4), 731 – 40.
- Carmeliet, P., Jain, R.K. 2000, Angiogenesis in cancer and other diseases. *Nature* 407: 249–57
- Chau, C.H., Clavijo, C.A., Deng, H.T *et al.* 2005. Etk/Bmx mediates expression of stress-induced adaptive genes VEGF, PAI-1, and iNOS via multiple signaling cascades in different cell systems. *Am J Physiol Cell Physiol*; 289: 444-454.
- Chesney, J., Metz, C., Stavitsky, A.B., Bacher, M., Bucala, R. 1998. Regulated production of type I collagen and inflammatory cytokines by peripheral blood fibrocytes. *J Immunol*. 160(1):419–425.
- Choi, Y.H., Kim, K.M., Kim, H.O., Jang, Y.C., Kwak, I.S. 2013. Clinical and Histological Correlation in Post-Burn Hypertrophic Scar for Pain and Itching Sensation. *Ann Dermatol*; 25(4): 428-433

- Clark, I.A. 2007. "How TNF was recognized as a key mechanism of disease," *Cytokine and Growth Factor Reviews*, vol. 18, no. 3-4, pp. 335–343.
- Clark, J.A., Turner, M.L., Howard, L., Stanescu, H., Kleta, R., Kopp, J.B. 2009. Description of Familial Keloids in Five Pedigrees : Evidence for Autosomal Dominant Inheritance and Phenotypic Heterogeneity. *BMC dermatology*; 1-9
- Czubryt, M.P. 2012. Common Threads in Cardiac Fibrosis, Infarct Scar Formation, and Wound Healing. *Fibrogenesis & Tissue Repair*; 5(19): 1-11
- Distler, J.H., Juñgel, A., Pileckyte, M., *et al.* 2007. Hypoxia induced increase in the production of extracellular matrix proteins in systemic sclerosis. *Arthritis Rheum.* 56: 4203.
- Duffy, A.M., Bouchier-Hayes, D.J., Harmey, J.H. 2000. Vascular Endothelial Growth Factor (VEGF) and Its Role in Non-Endothelial Cells: Autocrine Signalling by VEGF. *Madame Curie Bioscience Database*
- Edriss, A.S. 2005. Management of Keloid and Hypertrophic Scars. *Annals of Burns and Fire Disasters.* 18(4): 1-14
- Fajardo, L.F., Kwan, H.H., Kowalski, J., Prionas, S.D., Allison, A.C. Dual role of tumor necrosis factor- α in angiogenesis *Am. J. Pathol* 1992; 140:539–544.
- Freshney, R.I. 2005. Culture of animal cells: a manual of basic technique. *5th ed.* Willey and Son, Inc.
- Fujiwara, M., Muragaki, Y., Ooshima, A. 2005 : Keloid-derived fibroblasts show increased secretion of factors involved in collagen turnover and depend on matrix metalloproteinase for migration. *Br J Dermatol* 153: 295-200.
- Gabhann, F.M., Qutub, A.A., Annex, B.H., Popel, A.S. 2010. Systems biology of pro-angiogenic therapies targeting the VEGF System : *Wiley Interdiscip Rev Syst Biol Med.* 2010 ; 2(6): 694–707.
- García, A., Delgado, G. 2006, Constituents from *Tithonia diversifolia*. Stereochemical Revision of 2 α -Hydroxytirodunin. *J. Mex. Chem. Soc.* 50(4):180-3
- Gauglitz, G.G., Korting, H.C., Pavicic, T., Ruzicka, T., Jeschke, M.G. 2011. Hypertrophic Scarring and Keloids: Pathomechanisms and Current and Emerging Treatment Strategies. *Mol Med*; 17(1-2): 113-125

- Gira, A.K., Brown, L.F., Washington, C.V., Cohen, C., and Arbiser, J.L. 2004, Keloids demonstrate high-level epidermal expression of vascular endothelial growth factor. *J Am Acad Dermatol* 50:850–3
- Goffin, E., Ziemons, E., De Mol, P., de Madureira, C., Martins, A.P., da Cunha, AP., *et al.* 2002, In vitro antiplasmodial activity of *Tithonia diversifolia* and identification of its main active constituent : Tagitinin C, *Planta Medica*, 68 (6): 543-545.
- Gu, J.Q., Gills, J.J., Park, E.J., Mata-Greenwood, E., Hawthorne, M.E., and Axelrod, F., *et al.* 2002. Sesquiterpenoids from *Tithonia diversifolia* with Potential Cancer Chemopreventive Activity. *J. Nat. Prod.* 65 (4), pp 532–536.
- Gurtner, G.C., Werner, S., Barrandon, Y., Longaker, M.T. 2008, Wound repair and regeneration. *Nature* ; 453: 314–21.
- Halim, A.S., Emami, A., Salahshourifar, I., Kannan, T.P. 2012. Keloid Scarring: Understanding the Genetic Basis, Advances and Prospects. *Arch Plast Surg*; 39: 184-189
- Han, Y.P., Tuan, T.L., Wu, H., Hughes, M., Garner, W.L. 2001, TNF- α stimulates activation of pro-MMP2 in human skin through NF- κ B mediated induction of MT1-MMP. *J Cell Sci.* 114(Pt 1): 131–139.
- Hatamipur, E., Mehrabi, S., Hatamipoor, M. 2011, Effects of combined intralesional 5- fluorouracil and topical silicone in prevention of keloid: A double blind randomized clinical trial study. *Acta Medica Iranica.* 49(3): 127- 30.
- Hoeben, A., Landuyt, B., Highley, M.S., Wildiers, H., Van Oosterom, A.T., De Bruijn, E.A. 2004. Vascular endothelial growth factor and angiogenesis. *Pharmacol Rev* 56:549–580.
- Hutapea, J.R. 1994. Inventaris Tanaman Obat Indonesia. Jakarta: Badan Penelitian dan Pengembangan Kesehatan. Hal. 297.
- Johnson, K.E., Wilgus, T.A., 2014. Vascular Endothelial Growth Factor and Angiogenesis in the Regulation of Cutaneous Wound Repair. *Adv. Wound Care* 3, 647–661.
- Kakar, A.K., Shahzad, M., Haroon, T.S. 2006. Keloids: Clinical Features and Management. Part I. *Journal of Pakistan Association of Dermatologist*; 16: 97-103
- Keira, S.M, Ferreira, L.M., Gagnani, A., Duarte, I.S., Santos, I.A.N. 2004. Experimental model for fibroblast culture. *Acta Cir Bra.* 19:11- 6.

- Kischer, C.W. 1992. The microvessels in hypertrophic scars, keloids and related lesions: a review. *J Submicrosc Cytol Pathol* 24:281–296
- Kuroda, M., Yokosuka, A., Kobayashi, R., Jitsuno, M., Kando, H., Nosaka, K., Ishii, H., Yamori, T., Mimaki, Y., 2007. Sesquiterpenoids and flavonoids from the aerial parts of *Tithonia diversifolia* and their cytotoxic activity. *Chem.Pharm.Bull.* 55(8):1240-4.
- Kvanta, A., 1995. Expression and regulation of vascular endothelial growth factor in choroidal fibroblasts. *Curr. Eye Res.* 14, 1015–1020.
- Le, A.D., Zhang, Q., Wu, Y., Messadi, D.V., Akhondzadeh, A., Nguyen, A.L *et al.* 2004, Elevated vascular endothelial growth factor in keloids: relevance to tissue fibrosis. *Cells Tissues Organs* 176:87–94
- Lin, H.R., 2012. Sesquiterpene lactones from *Tithonia diversifolia* act as peroxisome proliferator-activated receptor agonists. *Bioorganic & medicinal chemistry letters*, 22(8), pp.2954–8.
- Lorquet, S., Berndt, S., Blacher, S., Gengoux, E., Peulen, O., Maquoi, E., *et al.* 2010. Soluble forms of VEGF receptor-1 and -2 promote vascular maturation via mural cell recruitment. *FASEB J.* 24:3782-3795.
- Louw, L 2007, "The keloid phenomenon : progres toward a solution", *Clin Anat*, vol.20, no. 1., pp. 3-14
- Madureira, M. C., Martins, A. P., Gomes, M., Paiva, J., Cunha, A. P., and Rosario, V., 2002. Antimalarial activity of medicinal plants used in traditional medicine in S. Tome and Principe islands. *J. Ethnopharmacol* 81:23 – 9.
- Mandela, Winnie., 2010. Pengaruh Senyawa Isolat Aktif Daun Kembang Bulan [*Tithonia diversifolia* (Hemsley) A. Gray] Terhadap Ekspresi Protein p53 Pada Sel HeLa Dengan Metode Imunositokimia [*Skripsi*], Fakultas Kedokteran Universitas Gadjah Mada, Yogyakarta.
- Mardihusodo, H.R., Wahyuningsih, M.S.H., Ardian, O.S., Empel, G.V., 2011. Sitotoksitas Campuran Ekstrak Etanol Daun Kembang Bulan (*Tithonia diversifolia* (HEMSLEY) A. GRAY.) dan Rimpang Kencur (*Kaempferia galanga* L.) pada Sel WiDR. *Majalah Obat Tradisional*, 16(3), 174 – 18.
- Mardihusodo, H.R., Wahyuningsih, M.S.H., Astuti, I. 2013. The effect of active compound isolated from the leaves of kembang bulan [*Tithonia diversifolia* (Hemsley) A. Gray] on cell cycle and angiogenesis of WiDR cell line. *J Med Sci*; 45(3): 101-111

- Mccarty, S.M., Syed, F., ayat, A. 2010. Influence of the Human Leukocyte Antigen Complex on the Development of Cutaneous Fibrosis : An Immunogenetic Perspective. *Acta Derm Venereol*; 90: 563-574
- Miller, M.C., Nanchahal, J. 2005. Advances in the Modulation of Cutaneous Wound Healing and Scarring. *Biodrug*; 19(6): 363-381
- Moronkola, D.O., Ogunwade, I.A., Walker, T.M., Setzer, W.N., and Oyewole, I.O., 2006. Identification of the main volatile compounds in the leaf and flower of *Tithonia diversifolia* (Hemsl) Gray. *J Nat Med* 61:63-66
- Motoyama, N., Naka, K. 2004. DNA damage tumor suppressor genes and genomic instability. *Curr opin genet dev* 14(1): 11-6.
- Muller, G.H., Robert, W.K., William, H.M., Craig, E.G. 2001. Muller & Kirk's Small Animal Dermatology 6th. Philadelphia: WB Saunders
- Muneuchi, G., Suzuki, S., Onodera, M. 2006, Long-term outcome of intralesional injection of triamcinolone acetonide for the treatment of keloid scars in Asian patients, *Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery*, 40 : 111-116.
- Mustoe, T.A, Cooter, R.D, Gold, M.H, Hobbs, R., Ramelet, A.A., Shakespeare, P.G., *et al.* 2002, : International clinical recommendations on scar management. *Plast Reconstr Surg* 110: 560-571.
- Nishida, N., Yano, H., Nishida, T., Kamura, T., Kojiro, M. 2006. *Angiogenesis in Cancer*. *Vasc Health Risk Manaq.* 2(3):213-19
- O'Kane, S. 2002. Wound remodelling and scarring. *J Wound Care* ; 11: 296-9.
- Obafemi, C.A., Sulaimon, T.O., Akinpelu, D.A., Olugbade, T.A. 2006. Anti microbial activity of extract and a germacranolide type sesquiterpene lactone from *Tithonia diversifolia* leaf extract. *African Journal of Biotechnology*. 5(12) : 1254-1258.
- Ogawa, R. 2011. Mechanobiology of Scarring. *Wound Rep Reg* ; 19: S2-S9
- Ohno, H., Shirato, K., Sakurai, T., Ogasawara, J., Sumitani, Y. 2012. Effect of exercise on HIF-1 and VEGF signaling. *JPFMSM*. 1(1): 5-16
- Otsuka, S., Tamiya, T., Ono, Y., Michiue, H., Kurozumi, K., Daido, S., *et al.* 2004. The relationship between peritumoral brain edema and the expression of vascular endothelial growth factor and its receptors in intracranial meningiomas. *J Neurooncol.* 70: 349-357.
- Paul, C., Maumus-Robert, S., Mazereeuw-Hautier, J., Guyen, C., Saudez, X., Schmitt, A. 2011. Prevalence and risk factors for xerosis in the elderly: a

- cross-sectional epidemiological study in primary care. *Dermatology*. 223(3): 260-5.
- Penn, J.W., Adriaan O.G., Kerstin, J.R. 2012. The role of the $\text{tgf-}\beta$ family in wound healing, burns and Scarring: a review article. *Int J Burn Trauma*. 2(1):18-28.
- Perdanakusuma, D.S. 2007. Anatomi Fisiologi Kulit Dan Penyembuhan Luka. Surabaya, *Prosiding From Caring to Curing, Pause Before You Use Gauze*, Airlangga University School Of Medicine – Dr. Soetomo General Hospital. Hal.1-8.
- Plate, K.H., Warnke, P.C. 1997. Vascular endothelial factor. *J Neurooncol*. 35: 365- 372.
- Ranti, I. 2014. Efek Antifibrotik Isolat Tagitinin C dari Daun Kembang Bulan [*Tithonia Diversifolia* (Hemsley) A. Gray]. *Tesis*. Universitas Gadjah Mada. Yogyakarta.
- Robles, D.T., Berg, D. 2007, Abnormal wound healing: keloids. *Clinics in Dermatology* ; 25: 26-32.
- Rungeler, P., Lyss, G., Castro, V., Mora, G., Pahl, H.L., Merfort, I. Study of three sesquiterpene lactones from *Tithonia diversifolia* on their anti-inflammatory activity using the transcription factor NF-kappa B and enzyme of the arachidonic acid pathway as target. *Planta med*. 1998. 64 588-593.
- Sadick, H., Herberger, A., Riedel, K., Bran, G., Goessler, U., Hoermann, K., Riedel, F. 2008. TGF- beta 1 antisense therapy modulates expression of matrix metalloproteinases in keloid derived fibroblasts. *Int J Mol Med* 22: 55-60.
- Saito, T., Takeda, N., Amiya, E., Nakao, T., Abe, H., Semba, H., *et al*. 2013. VEGF-A induces its negative regulator, soluble form of VEGFR-1, by modulating its alternative splicing. *FEBS Lett*. S0014-5793(13)00392-x
- Sanchez-Mendoza, M.E., Reyes-Ramirez, A., Antonio, L.C., Jimenez, L.M., Rodriguez-Silverio, J., Arrieta, J., 2011. Bioassay-guided isolation of an anti-ulcer compound, tagitinin c, from *Tithonia diversifolia*: role of nitric oxide, prostaglandins and sulfhydryls. *Molecules*: (16:665-674).
- Sayah, D.N., Soo, C., Shaw, W.W., Watson, J., Messadi, D., Longaker, M.T *et al*. 1999. Down regulation of apoptosis-related genes in keloid tissues. *J Surg Res* 87:209–16
- Seifert, O. 2008. "Keloid- A fibroproliferative Disease" (*dissertation*). Division of Dermatology Department of Clinical and Experimental Medicine Faculty

of Health Sciences: Lincoping University SE-58185 Linkoping Sweden;
13-17

Seifert, O., Mrowietz, U. 2009. Keloid Scarring : Bench and Bedside. *Arch Dermatol Res*; 301: 259-272

Seo, B.F., Lee, J.Y., and Jung, S.N. 2013. Models of Abnormal Scarring. *BioMed Research International*; Article ID 423147: 1-8

Shejbal, D., Bedekovic, V., Ivkic, M., Kolagjera, L., Aleric, Z., Drvis, P. 2004. Strategies in the Treatment of Keloid and Hypertrophic Scars. *Acta Clin Croat*. 43: 417-422

Shih, B., Garside, E., McGrouther, D.A., Bayat, A. 2010. Molecular Dissection of Abnormal Wound Healing Processes Resulting in Keloid Disease. *Wound Rep Reg*. 18: 139-153

Slemp, A.E., Kirsner, R.E. 2006. "Keloid and scars : a review of keloid and scars, their pathogenesis, risk factors, and management", *Curr Opin Pediatr*. 18(4): 396-402

Subowo. 2009, *Imunobiologi*. 10th ed. Bandung: *Angkasa* : 232

Tona, L., Kambu, K., Mesia, K., Cimanga, K., Apers, S., De Brynne, T., Pieters, L., Totte, J., and Vlietinck, A.J., 1999. Biological screening of traditional preparation from some medicinal plants used as antidiarrhoeal in Kinshasa Kongo. *Phytomedicine* 6(1): 59-66.

Tortora, G.J., Derrickson, B.H. 2009. Principles of Anatomy and Physiology. Twelfth Edition. Asia: *Wiley*: 5: 134-139

Tranggono, R.I., Fatma Latifah. 2007. *Buku Pegangan Ilmu Pengetahuan Kosmetik*, Editor: Joshita Djajadisastra. Jakarta: Penerbit Pustaka Utama. P.6-7

Urioste, S.S., Arndt, K.A., Dover., J.S. 1999. "Keloids and hypertrophic scars : revieww and treatment strategies", *Semin Cutan Med Surg*, 21(2): 159-171

Velnar, T., Bailey, T., Smrkolj. 2009. The Wound Healing Process : An Overview of the Cellular and Molecular Mechanisms. *The Journal of International Medical Research*: 37: 1528-1542

Wahyuningsih, M.S.H., Wijayanti, M.A. 2009. Isolation and identification of anticancer compounds active fraction *Tithonia diversifolia* (Hemsley) A. Gray, selectivity and mechanism of apoptosis in vitro. Research Reports of Medical Science Research Development. Yogyakarta, Indonesia: Faculty of Medicine, University of Gadjah Mada.

- Wahyuningsih, M.S.H., Widodo, Y., Hidayat, R., A. Sadid. 2015. Antifibrotic effect of standardized ethanol extract of *Tithonia diversifolia* (Hemsley) A. Gray on keloid fibroblasts. *Int J Pharm Pharm Sci*; 7(4): 642-647
- Wahyuningsih, M.S.H., Wijayanti, M.A., Budiyanto, A., Muhammad Hanafi, 2015, Isolation and Identification of Potential Cytotoxic Compound from Kembang Bulan [*Tithonia diversifolia* (Hemsley) A. Gray] Leaves, *Int J Pharm Pharm Sci*; 7(6): 298-301
- Wall, S.J., Bevan, D., Thomas, D.W., Harding, K.G., Edwards, D.R., Murphy, G. 2002. Differential expression of matrix metalloproteinases during impaired wound healing of the diabetic mouse. *J Invest Dermatol* 119: 91-98.
- Wang, X.Q., Lu, S.L., Mao, Z.G., Liu, Y.K., 2007. Study on the biological function of vascular endothelial cells in the hypertrophic scar. Article in Chinese. *Zhonghua Shao Shang Za Zhi*. 23(3):219-21.
- Wilgus, T.A., Ferreira, A.M., Oberyszyn, T.M., Bergda, V.K., DiPietro, L.A., 2008. Regulation of scar formation by vascular endothelial growth factor. *Lab Invest*. 88(6): 579–590.
- Wolfram, D., Tzankov, A., Pulzl, P., Piza-Katzer, H. 2009. Hypertrophic Scars and Keloids—A Review of Their Pathophysiology, Risk Factors and Therapeutic Management. *Dermatol Surg*; 35: 171-181
- Wu, W.S., Wang, F.S., Yang, K.D., Haung, C.C., Dacks, J.M., Kuo, Y.R. Dexamethasone induction of keloid regression through effective suppression of VEGF expression and keloid fibroblast proliferation. *J Invest Dermatol* 2006;126:1264–71.
- Xu, S., Li, D., Teng, J., *et al*, 2007, Effects of steroids, interferon-2B, or interleukin 1B on apoptosis of fibroblasts from keloid, hypertrophic scars, and normal skin and related signal pathway, *European Journal of Plastic Surgery*, vol. 30, p.159–167.
- Zhang, Q., Wu, Y., Ann, D.K., Messadi, D.V., Tuan, T.L., Kelly, A.P., Bertolami, C.N, Le, A.D. 2003. Mechanisms of hypoxic regulation of plasminogen activator inhibitor-1 gene expression in keloid fibroblasts. *J Invest Dermatol* 121: 1005-1012.
- Ziemer, L.S., Koch, C.J., Maity, A., Magarelli, D.P., Horan, A.M., Evans, S.M. 2001. Hypoxia and VEGF mRNA expression in human tumors. *Neoplasia*. 3(6):500-8
- Ziemons, E., Goffin, E., Lejeune, R., Angenot, L., Thunus, L., 2004. Supercritical fluid extraction of tagitinin C from *tithonia diversifolia*: Comparison of