

## DAFTAR PUSTAKA

- Abass, H., Kamel, R., Abdelbary, A., 2012. Metronidazole bioadhesive vaginal suppositories: Formulation, in vitro and in vivo evaluation. *Int. J. Pharm. Pharm. Sci.* 4, 344–353.
- Abd Ellah, N.H., Abdel-Aleem, J.A., Abdo, M.N., Abou-Ghadir, O.F., Zahran, K.M., Hetta, H.F., 2019. Efficacy of ketoconazole gel-flakes in treatment of vaginal candidiasis: Formulation, in vitro and clinical evaluation. *Int. J. Pharm.* 567, 118472.
- Aiyalu, R., Govindarjan, A., Ramasamy, A., 2016. Formulation and evaluation of topical herbal gel for the treatment of arthritis in animal model. *Brazilian J. Pharm. Sci.* 52.
- Al Khateb, K., Ozhmukhametova, E.K., Mussin, M.N., Seilkhanov, S.K., Rakhypbekov, T.K., Lau, W.M., Khutoryanskiy, V. V., 2016. In situ gelling systems based on Pluronic F127/Pluronic F68 formulations for ocular drug delivery. *Int. J. Pharm.* 502, 70–79.
- Bain, M.K., Maity, D., Bhowmick, B., Mondal, D., Mollick, M.M.R., Sarkar, G., Bhowmik, M., Rana, D., Chattopadhyay, D., 2013. Effect of PEG-salt mixture on the gelation temperature and morphology of MC gel for sustained delivery of drug. *Carbohydr. Polym.* 91, 529–536.
- Beck-Sague, C., Beck, C., 2004. *Deadly Disease and Epidemics HIV/AIDS*. Chelsea House Publisher, United States of America.
- Boddupalli, B.M., Mohammed, Z.N.K., Nath A., R., Banji, D., 2010. Mucoadhesive drug delivery system: An overview. *J. Adv. Pharm. Technol. Res.* 1, 381–387.
- Bonacucina, G., Cespi, M., Mencarelli, G., Giorgioni, G., Palmieri, G.F., 2011. Thermosensitive self-assembling block copolymers as drug delivery systems. *Polymers (Basel)*. 3, 779–811.
- Chen, Y., Lee, J.H., Meng, M., Cui, N., Dai, C.Y., Jia, Q., Lee, E.S., Jiang, H.B., 2021. An overview on thermosensitive oral gel based on poloxamer 407. *Materials (Basel)*. 14.
- Cook, Sarah Louise, Cook, Sarah L, Bull, S.P., Methven, L., Parker, J.K., Khutoryanskiy, V. V, 2017. Mucoadhesion : A food perspective. *Food Hydrocoll.* 72, 281–296.
- D'souza, A.A., Shegokar, R., 2016. Polyethylene glycol (PEG): a versatile polymer for pharmaceutical applications. *Expert Opin. Drug Deliv.* 13, 1257–1275.
- das Neves, J., Bahia, M.F., 2006. Gels as vaginal drug delivery systems.

*Int. J. Pharm.* 318, 1–14.

- Das Neves, J., Rocha, C.M.R., Gonçalves, M.P., Carrier, R.L., Amiji, M., Bahia, M.F., Sarmiento, B., 2012. Interactions of microbicide nanoparticles with a simulated vaginal fluid. *Mol. Pharm.* 9, 3347–3356.
- Dodge, A., Gould, P.L., 1987. Dissolution of Chlorpropamide Tablets in a Methanol-Water Binary Solvent System. *Drug Dev. Ind. Pharm.* 13, 1817–1826.
- Dyja, R., Jankowski, A., 2017. The Effect of Additives on Release and In vitro Skin Retention of Flavonoids from Emulsion and Gel Semisolid Formulation. *Int. J. Cosmet. Sci.* 39, 442–449.
- European Medicine Agency, E.M.A., 2020. Vocabria. Netherlands.
- Ferguson, L.M., Rohan, L.C., 2008. The importance of the vaginal delivery route for antiretrovirals in HIV prevention. *Ther. Deliv.* 2, 1535–1550.
- Ferguson, L.M., Rohan, L.C., 2011. The Importance of the Vaginal Delivery Route for Antiretrovirals in HIV Prevention. *Ther. Deliv.* 2, 1535–1550.
- Galgatte, U.C., Kumbhar, A.B., Chaudhari, P.D., 2014. Development of in situ gel for nasal delivery: Design, optimization, in vitro and in vivo evaluation. *Drug Deliv.* 21, 62–73.
- Güven, U.M., Berkman, M.S., Şenel, B., Yazan, Y., 2010. in situ gelling systems for ocular allergy. *Brazilian J. Pharm. Sci.*
- Hassounah, S.A., Alikhani, A., Oliveira, M., Bharaj, S., Ibanescu, R.-I., Osman, N., Xu, H.-T., Brenner, B.G., Mesplède, T., Wainberga, M.A., 2017. Antiviral Activity of Bictegrovir and Cabotegrovir against Integrase Inhibitor- Resistant SIVmac239 and HIV-1 61, 1–9.
- Huang, H., Qi, X., Chen, Y., Wu, Z., 2019. Thermo-sensitive hydrogels for delivering biotherapeutic molecules: A review. *Saudi Pharm. J.* 27, 990–999.
- Islam, M.T., Ciotti, S., Ackermann, C., 2004. Rheological Characterization of Topical Carbomer Gels Neutralized to Different pH 21, 1192–1199.
- Karim, S.S.A., Kashuba, A.D., Werner, L., Karim, Q.A., 2011. Drug Concentrations After Topical and Oral Antiretroviral Pre-exposure Prophylaxis: Implications for HIV Prevention in Women. *Lancet* 378, 279–281.
- Kaur, R., Sharma, P., Gupta, G.K., Ntie-Kang, F., Kumar, D., 2020. Structure-activity-relationship and mechanistic insights for anti-HIV

natural products. *Molecules* 25, 1–48.

- Khattab, A., Marzok, S., Ibrahim, M., 2019. Development of optimized mucoadhesive thermosensitive pluronic based in situ gel for controlled delivery of Latanoprost: Antiglaucoma efficacy and stability approaches. *J. Drug Deliv. Sci. Technol.* 53, 101134.
- Kovač, L., Časar, Z., 2020. A Literature Review of the Patent Application Publications on Cabotegravir—an HIV Integrase Strand Transfer Inhibitor. *Expert Opin. Ther. Pat.* 30, 195–208.
- Kummar, V., Abbas, A.K., Aster, J.C., 2015. *Robbins and Cotran: Pathologic Basic of Disease Ninth Edition, 9th ed.* Elsevier Saunders, Philadelphia.
- Liebert, M.A., 1988. Final Report on the Safety Assessment of DMDM Hydantoin. *Int. J. Toxicol.* 7, 245–277.
- Liu, S., Bao, H., Li, L., 2015. Role of PPO-PEO-PPO triblock copolymers in phase transitions of a PEO-PPO-PEO triblock copolymer in aqueous solution. *Eur. Polym. J.* 71, 423–439.
- M.A. Fathalla, Z., Vangala, A., Longman, M., Khaled, K.A., Hussein, A.K., El-Garhy, O.H., Alany, R.G., 2017. Poloxamer-based thermoresponsive ketorolac tromethamine in situ gel preparations: Design, characterisation, toxicity and transcorneal permeation studies. *Eur. J. Pharm. Biopharm.* 114, 119–134.
- Machado, R.M., Palmeira-de-Oliveira, A., Gaspar, C., Martinez-de-Oliveira, J., Palmeira-de-Oliveira, R., 2015. Studies and methodologies on vaginal drug permeation. *Adv. Drug Deliv. Rev.* 92, 14–26.
- Majeed, A., Khan, N.A., 2019. Ocular in situ gel: An overview. *J. Drug Deliv. Ther.* 9, 337–347.
- Manna, S., Lakshmi, U.S., Racharla, M., Sinha, P., Kanthal, L.K., Kumar, S.P.N., 2016. Bioadhesive HPMC gel containing gelatin nanoparticles for intravaginal delivery of tenofovir. *J. Appl. Pharm. Sci.* 6, 22–29.
- Mc Crudden, M.T.C., Larrañeta, E., Clark, A., Jarrahian, C., Rein-Weston, A., Creelman, B., Moyo, Y., Lachau-Durand, S., Niemeijer, N., Williams, P., McCarthy, H.O., Zehring, D., Donnelly, R.F., 2019. Design, Formulation, and Evaluation of Novel Dissolving Microarray Patches Containing Rilpivirine for Intravaginal Delivery. *Adv. Healthc. Mater.* 8.
- Mcperson, T.D., Sobieszczyk, M.E., Markowitz, M., 2018. Cabotegravir in the treatment and prevention of Human Immunodeficiency Virus-1.

*Expert Opin. Investig. Drugs* 27, 413–420.

- Mohanty, D., Simharaju, N., Haque, M.A., Sahoo, C.K., Telangana, H., Telangana, H., Telangana, H., Telangana, H., 2018. Review Article A Review on in situ Gel: A Novel Drug Delivery System. *Int. J. Pharm. Sci. Rev. Res.* 50, 175–181.
- Naif, H.M., 2013. Pathogenesis of HIV infection. *Infect. Dis. Rep.* 5, 26–30.
- Nyamweya, S., Hegedus, A., Jaye, A., Rowland-jones, S., Flanagan, K.L., Macallan, D.C., 2013. Comparing HIV-1 and HIV-2 infection : Lessons for viral immunopathogenesis. *Rev. Med. Virol* 23, 221-240.
- Oliveira, M., Ibanescu, R.I., Anstett, K., Mésplède, T., Routy, J.P., Robbins, M.A., Brenner, B.G., Legault, M., Baril, J.G., Charest, L., Charron, M.A., Côté, P., de Pokomandy, A., Dufresne, S., Fortin, C., Friedman, J., Gilmore, N., Huchet, E., Klein, M., Labreque, L., Lalonde, R., Leblanc, R., Lessard, B., Milne, C., Munoz, M., Potter, M., Rouleau, D., Szabo, J., Thomas, R., Tremblay, C., Trottier, B., Vézina, S., 2018. Selective resistance profiles emerging in patient-derived clinical isolates with cabotegravir, bictegravir, dolutegravir, and elvitegravir. *Retrovirology* 15, 1–14.
- Orkin, C., Arasteh, K., Górgolas Hernández-Mora, M., Pokrovsky, V., Overton, E.T., Girard, P.-M., Oka, S., Walmsley, S., Bettacchi, C., Brinson, C., Philibert, P., Lombaard, J., St. Clair, M., Crauwels, H., Ford, S.L., Patel, P., Chounta, V., D'Amico, R., Vanveggel, S., Dorey, D., Cutrell, A., Griffith, S., Margolis, D.A., Williams, P.E., Parys, W., Smith, K.Y., Spreen, W.R., 2020. Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection. *N. Engl. J. Med.* 382, 1124–1135.
- Owen, D.H., Katz, D.F., 1999. A vaginal fluid simulant. *Contraception* 59, 91–95.
- Patel, P., Ford, S.L., Lou, Y., Bakshi, K., Tenorio, A.R., Zhang, Z., Pan, R., Spreen, W., 2019. Effect of a High-Fat Meal on the Pharmacokinetics of the HIV Integrase Inhibitor Cabotegravir. *Clin. Pharmacol. Drug Dev.* 8, 443–448.
- Permana, A.D., Utami, R.N., Courtenay, A.J., Manggau, M.A., Donnelly, R.F., Rahman, L., 2020. Phytosomal nanocarriers as platforms for improved delivery of natural antioxidant and photoprotective compounds in propolis: An approach for enhanced both dissolution behaviour in biorelevant media and skin retention profiles. *J. Photochem. Photobiol. B Biol.* 205, 111846.
- Permana, A.D., Utami, R.N., Layadi, P., Himawan, A., Juniarti, N., Anjani, Q.K., Utomo, E., Mardikasari, S.A., Arjuna, A., Donnelly, R.F., 2021a.

Thermosensitive and mucoadhesive in situ ocular gel for effective local delivery and antifungal activity of itraconazole nanocrystal in the treatment of fungal keratitis. *Int. J. Pharm.* 602, 120623.

- Permana, A.D., Utomo, E., Pratama, M.R., Amir, M.N., Anjani, Q.K., Mardikasari, S.A., Sumarheni, S., Himawan, A., Arjuna, A., Usmanengsi, U., Donnelly, R.F., 2021b. Bioadhesive-Thermosensitive in Situ Vaginal Gel of the Gel Flake-Solid Dispersion of Itraconazole for Enhanced Antifungal Activity in the Treatment of Vaginal Candidiasis. *ACS Appl. Mater. Interfaces* 13, 18128–18141.
- Radzio-basu, J., Council, O., Cong, M., Ruone, S., Newton, A., Wei, X., Mitchell, J., Ellis, S., Petropoulos, C.J., Huang, W., Spreen, W., Heneine, W., García-Ierma, J.G., 2019. pre-exposure prophylaxis during acute. *Nat. Commun.* 1–8.
- Regina, R., Pereira, D.A., Bruschi, M.L., 2012. Vaginal mucoadhesive drug delivery systems. *Drug Dev. Ind. Pharm.* 38, 643–652.
- Rençber, S., Karavana, S.Y., Şenyiğit, Z.A., Eraç, B., Limoncu, M.H., Baloğlu, E., 2017. Mucoadhesive in situ Gel Formulation for Vaginal Delivery of Clotrimazole: Formulation, Preparation, and in vitro/in vivo Evaluation. *Pharm. Dev. Technol.* 22, 551–561.
- Riono, P., Challacombe, S.J., 2020. HIV in Indonesia and in Neighbouring Countries and Its Social Impact. *Oral Dis.* 26, 28–33.
- Rodriguez-Garcia, M., 2020. How HIV exploits T cells in the endometrium. *eLife* 1–4.
- Rodriguez-Garcia, M., Connors, K., Ghosh, M., 2021. HIV Pathogenesis in the Human Female Reproductive Tract. *Curr. HIV/AIDS Rep.* 18, 139–156.
- Rohan, L.C., Sassi, A.B., 2009. Vaginal drug delivery systems for HIV prevention. *AAPS J.* 11, 78–87.
- Rossi, E., Meuser, M.E., Cunanan, C.J., Cocklin, S., 2021. Structure, function, and interactions of the hiv-1 capsid protein. *Life* 11, 1–25.
- Rowe, R.C., Sheskey, P.J., Quinn, M.E., 2009. *Handbook of Pharmaceutical Excipients 6th Edition*. Pharmaceutical Press and American Pharmacists Association., London.
- Russo, E., Villa, C., 2019. Poloxamer Hydrogels for Biomedical Applications. *Pharmaceutics* 11, 671.

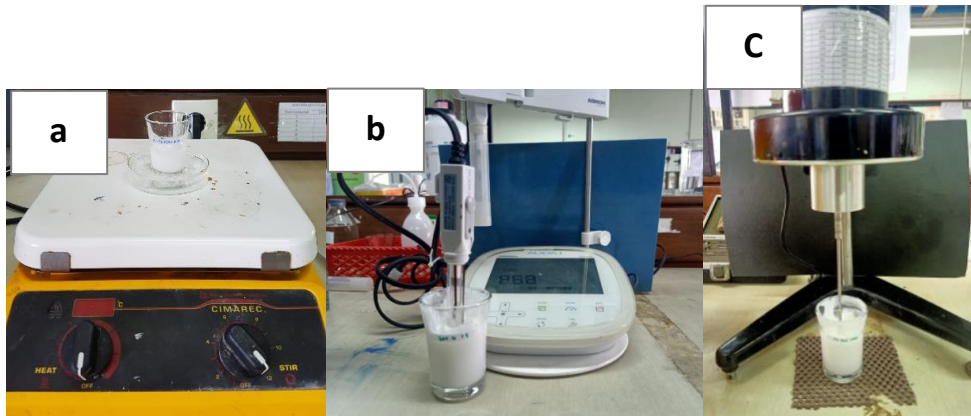
- Sahoo, C.K., Kumar Nayak, P., Sarangi, D.K., Sahoo, T.K., 2013. Intra Vaginal Drug Delivery System: An Overview. *Am. J. Adv. Drug Deliv.* 1, 43–45.
- Schwarz, J.C., Pagitsch, E., Valenta, C., 2013. Comparison of ATR-FTIR spectra of porcine vaginal and buccal mucosa with ear skin and penetration analysis of drug and vehicle components into pig ear. *Eur. J. Pharm. Sci.* 50, 595–600.
- Sepulveda-Crespo, D., Jimenez-Fuentes, J.L., Munoz-Fernandez, M.A., 2019. *Drug Delivery Nanosystems From Bioinspiration and Biomimetics to Clinical Applications*. In: Demetzos, C., Pispas, S., Pippa, N. (Eds.), . Pan Stanfors Publishing, Singapore.
- Shah, SNH, Tahir, M., Safdar, A., Riaz, R., Shahzad, Y., Rabbani, M., Karim, S., Murtaza, G., 2013. Effect of Permeation Enhancers on the Release Behaviour and Permeation Kinetics of Novel Tramadol Lotions. *Trop. J. Pharm. Research* 12, 27–32.
- Singal, A., Grover, C., 2015. *Comprehensive Approach to Infections in Dermatology*, 2015th ed. Jaypee Brother Medical Publishers (P) Ltd, India.
- Solar, O., Gunasekaran, S., 2010. Rheological properties of rennet casein-whey protein gels prepared at different mixing speeds. *J. Food Eng.* 99, 338–343.
- Soliman, G.M., Fetih, G., M, A.A., 2016. Thermosensitive Bioadhesive Gels for The Vaginal Delivery of Sildenafil Citrate: In Vitro Characterization and Clinical Evaluation in Women Using Clomphene Citrate for Induction of Ovulation, *Drug Development and Industrial Pharmacy*. Taylor & Francis.
- Squier, C.A., Mantz, M.J., Schlievert, P.M., Davis, C.C., 2008. Porcine Vagina Ex Vivo as a Model for Studying Permeability and Pathogenesis in Mucosa. *J. Pharm. Sci.* 97, 9–21.
- Subramanian, P., 2021. Mucoadhesive delivery system: A smart way to improve bioavailability of nutraceuticals. *Foods* 10.
- Tebit, D.M., Ndembi, N., Weinberg, A., Quinones-Mateu, M., 2012. Mucosal transmission of human immunodeficiency virus. *NIH Public Access* 10, 3–8.
- Trezza, C., Ford, S.L., Spreen, W., Pan, R., Piscitelli, S., 2015. Formulation and pharmacology of long-acting cabotegravir. *Curr. Opin. HIV AIDS* 10, 239–245.
- Tuçcu-Demiröz, F., Acartürk, F., Erdoğan, D., 2013. Development of Long-

acting Bioadhesive Vaginal Gels of Oxybutynin: Formulation, in vitro and in vivo Evaluations. *Int. J. Pharm.* 457, 25–39.

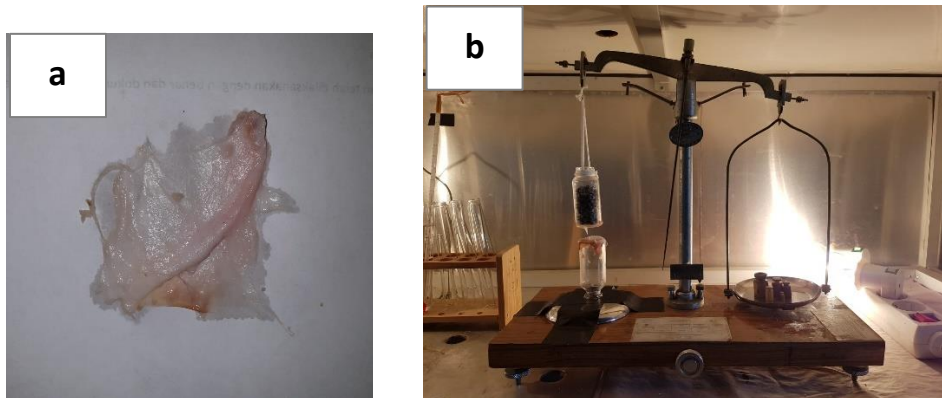
- Vigani, B., Faccendini, A., Rossi, S., Sandri, G., Bonferoni, M.C., Grisoli, P., Ferrari, F., 2019. Development of a Mucoadhesive In Situ Gelling Formulation for the Delivery of *Lactobacillus gasseri* into Vaginal Cavity. *J. Pharm.*
- Wang, Y., Lai, S.K., Suk, J.S., Pace, A., Cone, R., Hanes, J., 2008. Addressing the PEG Mucoadhesivity Paradox to Engineer Nanoparticles that “ Slip ” through the Human Mucus Barrier \*\*. *Wiley Intersci.* 9726–9729.
- Yenil, Ö., Kahraman, E., Algin Yapar, E., Cevher, E., Özkirimli, S., Özsoy, Y., 2013. Preparation and evaluation of bioadhesive inserts containing Verapamil hydrochloride for nasal delivery. *Lat. Am. J. Pharm.* 32, 1170–1177.
- Yu, T., Malcolm, K., Woolfson, D., Jones, D.S., Andrews, G.P., 2011. Vaginal gel drug delivery systems: Understanding rheological characteristics and performance. *Expert Opin. Drug Deliv.* 8, 1309–1322.
- Zulfiqar, H.F., Javed, A., Sumbal, A., Afroze, B., Ali, Q., Akbar, K., Nadeem, T., Rana, M.A., Nazar, Z.A., Nasir, I.A., Husnain, T., 2017. HIV Diagnosis and Treatment through Advanced Technologies. *Front. Public Heal.* 5, 1–16.

## LAMPIRAN

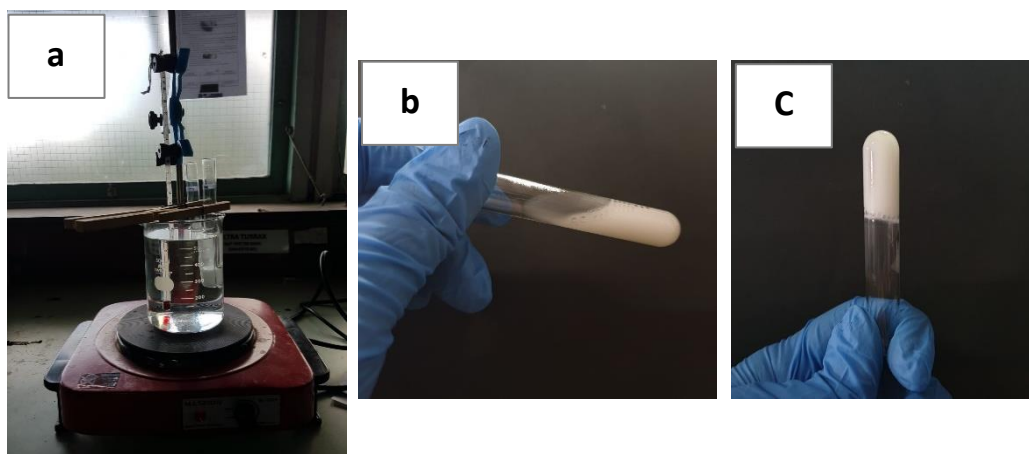
### Lampiran 1. Dokumentasi Penelitian



Gambar 24. (a) Proses formulasi gel termosensitif-mukoadhesif, (b) Evaluasi pH, dan (c) Evaluasi viskositas dan reologi



Gambar 25. (a) Mukosa vagina babi dan (b) Uji kekuatan mukoadhesif



Gambar 26. (a) Uji suhu gelasi, (b) Sediaan gel sebelum mengalami gelasi, dan (c) Sediaan setelah mengalami gelasi





**Gambar 27. Spektrofotometer Uv-Vis**