BAB 5
KESIMPULAN DAN SARAN

5.1. Kesimpulan

Dari hasil diatas dapat menjawab tujuan dari penelitian ini bahwa :

Setiap polimer dalam penelitian ini berpengaruh terhadap hidrogel seperti yang ditunjukkan dalam berbagai pengujian, baik tiap polimer itu sendiri maupun gabungan antar polimer. Untuk polimer chitosan, bersifat menaikkan atau memberikan pengaruh pada pengujian pengembangan, *swelling ratio*, *loading* obat, dan efisiensi enkapsulasi kecuali pada pengujian disolusi. Untuk polimer natrium alginat dan gabungan polimer chitosan-natrium alginat, bersifat menurunkan atau tidak memberikan pengaruh pada pengujian pengembangan, *swelling ratio*, *loading* obat, efisiensi enkapsulasi, dan disolusi.

Konsentrasi optimum yang didapat berdasarkan *design expert* ini adalah chitosan dengan konsentrasi 0,10 dan natrium alginat dengan konsentrasi 0,10. Formula D merupakan formula yang terpilih dalam dapar pH 2,1 sedangkan formula C merupakan formula yang terpilih dalam dapar pH 7,4.

5.2. Saran

Dapat dilakukan penelitian lebih lanjut terhadap hidrogel yang formulasikan ke dalam suatu bentuk sediaan misalnya tablet, *patch*, ataupun sediaan lainnya. Selain itu juga dapat dilakukan penelitian mengenai pelepasan suatu obat dari dalam suatu sediaan yang diformulasikan tanpa hidrogel dan yang diformulasikan dengan hidrogel. Selain itu juga dapat dilakukan penelitian mengenai pengaruh berbagai polimer lainny dan juga dengan bahan aktif yang berbeda, apakah berpengaruh atau tidak jika diformulasikan dengan hidrogel.

DAFTAR PUSTAKA

Amin, S., S. Rajabnezhad and K. Kohli, 2009, Hydrogels as Potential Drug Delivery Systems, **Scientific Research and Essay,** 3(11), 1175-1183.

Anal, K. A. and W. F. Stevens, 2005, Chitosan–Alginate Multilayer Beads for Controlled Release of Ampicillin, **International Journal of Pharmaceutics,** 290, 45–54.

Anonim, 1995, **Farmakope Indonesia**, ed. 4, Departemen Kesehatan Republik Indonesia, Jakarta, 1210.

Ansel, H. C., 1989, **Pengantar Bentuk Sediaan Farmasi**, edisi 4, terjemahan F. Ibrahim, Penerbit Universitas Indonesia, Jakarta, 291-292.

Banakar, U. V., 1992, **Pharmaceutical Dissolution Testing**, Marcel Dekker, Inc., New York, 20-21, 299-301.

Bennett, P. N. and M. J. Brown, 2003, **Clinical Pharmacology**, 9th ed., Churchill Livingstone, Spain, 282-285.

Bodek, K. H., 2006, Microcrystalline Chitosan as Pharmaceutical Preparation, ***Polish Chitin Society Monograph XI,*** *85-94.*

Bolton, S. and C. Bon, 2004, **Pharmaceutical Statistics Practical and Clinical Applications**, 4th ed., Marcel Dekker, Inc., New York, 265–270, 506–518.

Bravo, S. A., M. C. Lamas and C. J. Salomón, 2002, In-Vitro Studies of Diclofenac Sodium Controlled-release from Biopolymeric Hydrophilic Matrices, **J Pharm Pharmaceut Sci,** 5(3), 213-219.

Chowdhury, J. A., S. T. Jahan, Md. M. Morshed, J. Mallick, A. K. Nath, Md. Z. Uddin, M. Dutta, K. Islam and Md. H. Kawsar, 2011, Development and Evaluation of Diclofenac Sodium Loaded Alginate Cross-Linking Beads, **Bangladesh Pharmaceutical Journal,** 14(1), 41-48.

Coviello, T., P. Matricardi, C. Marianecci and F. Alhaique, 2007, Polysaccharide Hydrogels for Modified Release Formulations, **Journal of Controlled Release,** 119, 5–24.

Dai, Y., P. Li, J. Zhang, A. Wang and Q. Wei, 2007, Swelling Characteristics and Drug Delivery Properties of Nifedipine-Loaded pH Sensitive Alginate–Chitosan Hydrogel Beads, **Journal of Biomedical Materials Research Part B: Applied Biomaterials,** 493-500.

Datta, A., 2007, **Characterization of Polyethylene Glycol Hydrogels for Biomedical Applications**, thesis, University of Pune, India, 1-21.

Dumitriu, R. P., A. Oprea and C. Vasile, 2009, A Drug Delivery System Based on Stimuli-Responsive Alginate/N-Isopropylacryl Amide Hydrogel, **Cellulose Chemistry And Technology Cellulose Chem. Technol.,** 43(7-8), 251-262.

El-Leithy, E. S., D. S. Shaker, M. K. Ghorab and R. S. Abdel-Rashid, 2010, Evaluation of Mucoadhesive Hydrogels Loaded with Diclofenac Sodium–Chitosan Microspheres for Rectal Administration, **AAPS PharmSciTech,** 11(4), 1695-1702.

Ganji, F. and E. V-Farahani, 2008, Hydrogels in Controlled Drug Delivery Systems, **Iranian Polymer Journal,** 18(1), 63-88.

Ghosal, K. and S. D. Ray, 2011, Alginate/Hydrophobic HPMC (60M) Particulate Systems: New Matrix for Site-Specific and Controlled Drug Delivery, **Brazilian Journal of Pharmaceutical Sciences,** 47(4), 833-844.

Gonçalves, V. L., M. C. M. Laranjeira and V. T. Fávere, 2005, Effect of Crosslinking Agents on Chitosan Microspheres in Controlled Release of Diclofenac Sodium, **Polímeros: Ciência e Tecnologia,** 15(1), 6-12.

Green J. H., 1996, A Practical Guide to Analytical Method Validation, **Analytical Chemistry,** 23, 305-309.

Gulrez, S. K. H., S. Al-Assaf and G. O. Phillips, 2011, Hydrogels: Methods of Preparation, Characterisation and Applications, **Progress in Molecular and Environmental Bioengineering from Analysis and Modeling to Technology Applications,** 117-150.

Gupta, P., K. Vermani and S. Garg, 2002, Hydrogels: from Controlled Release to pH-Responsive Drug Delivery, **DDT,** 7(10), 569-579.

Hasan, S. M. F., T. Ahmed, N. Talib and F. Hasan, 2005, Pharmacokinetics of Diclofenac Sodium in Normal Man, **Pakistan Journal of Pharmaceutical Sciences,** 18(1), 18-24.

Hosseinzadeh, H., 2010, Controlled release of diclofenac sodium from pH-responsive carrageenan-g-poly(acrylic acid) superabsorbent hydrogel, **J. Chem. Sci.,** 122(4), 651–659.

Idkaidek, N. M., G. L. Amidona, D. E. Smitha, N. M. Najibb and M. M. Hassanc, 1998, Determination of the Population Pharmacokinetic Parameters of Sustained-Release and Enteric-Coated Oral Formulations, and the Suppository Formulation of Diclofenac Sodium by Simultaneous Data Fitting Using NONMEM, **Biopharm. Drug Dispos.,** 19, 169–174.

Katzung, B. G., 2002, **Farmakologi Dasar dan Klinik**, terjemahan D. Sjabana, E. Isbandiati, A. Basori, M. Soedjak, I. Uno, Ramadhani, dan S. Zakaria, Salemba Medika, Jakarta, 449- 462.

Korkiatithaweechai, S., P. Umsarika, N. Praphairaksit and N. Muangsin, 2011, Controlled Release of Diclofenac from Matrix Polymer of Chitosan and Oxidized Konjac Glucomannan, **Mar. Drugs,** 9, 1649-1663.

Kuru, E. A., N. Orakdogen and O. Okay, 2007, Preparation of Homogeneous Polyacrylamide Hydrogels by Free-Radical Crosslinking Copolymerization, **European Polymer Journal,** 43, 2913–2921.

Lin, C. and A. T. Metters, 2006, Hydrogels in Controlled Release Formulations: Network Design and Mathematical Modeling, **Advanced Drug Delivery Reviews,** 58, 1379-1408.

Lukman, A., 2011, **Pemanfaatan Pati Beras Ketan Pragelatinasi Sebagai Matriks Tablet Lepas Lambat Natrium Diklofenak dan Kaptopril Artikel**, tesis, Universitas Andalas, Padang.

Martin, A., J. Swarbick and A. Cammarata, 2008, **Farmasi Fisik Dasar-Dasar Kimia Fisik dalam Ilmu Farmasetik**, edisi ketiga, terjemahan Yoshita, Penerbit Universitas Indonesia, Jakarta, 845-848.

Motwani, S. K., S. Chopra, S. Talegaonkar, K. Kohli, F. J. Ahmad and R. K. Khar, 2008, Chitosan–Sodium Alginate Nanoparticles as Submicroscopic Reservoirs for Ocular Delivery:Formulation, Optimisation and In Vitro Characterisation, **European Journal of Pharmaceutics and Biopharmaceutics,** 68, 513–525.

Mozayani, A. and L.P. Raymon, 2004, **Handbook of Drug Interaction A clinical and Forensic Guide**, Humana Press, New Jersey, 337-339.

Neal, M. J., 2002, **Medical Pharmacology at a Glance**, 4th ed., Blackwell Science, London, 70-72.

Ottenbrite, R. M., 2010, **Biomedical Applications of Hydrogels Handbook**, Springer, New York, 147-154.

Park, H. and K. Park, 1994, Polymers in Pharmaceutical Products, **In Polymers of Biological and Biomedical Significance**, 8.

Patil, J. S., M. V. Kamalapur, S. S. Shiralshetti and D. V. Kadam, 2011, Ionotropically Gelled Chitosan-Alginate Complex Hydrogel Beads:Preparation, Characterization and *In-vitro* Evaluation, **Indian Journal of Pharmaceutical Education and Research,** 46(3), 248-252.

Patil, S. A., B. R. Rane, S. R. Bakliwal and S. P. Pawar, 2011, Pragmatic Hydrogels, **IJRAP 2011,** 2(3), 758-766.

Perrie, Y. and T. Rades, 2010, **FASTtrack Pharmaceutics-Drug Delivery and Targeting**, Pharmaceutical Press, London, 10-12.

Remington, J. P., 2001, **Remington The Science and Practice of Pharmacy,** 20th ed., Lippincott Williams and Wilkins, United States of America, 1040, 1056.

Rohindra, D. R., A. V Nand and J. R. Khurma, **Swelling Properties of Chitosan Hydrogels**, 32-35.

Rowe, R. C., P. J. Sheskey and S. C. Owen, 2006, **Handbook of Pharmaceutical Excipients**, 5th ed., Pharmaceutical Press, London, 159, 656.

Sabitha, P., J. V. Ratna and K. R. Reddy, 2010, Design and Evaluation of Controlled Release Chitosan-Calcium Alginate Microcapsules of Anti Tubercular Drugs for Oral Use, **International Journal of ChemTech Research,** 2(1), 88-98.

Satish, C. S., K. P. Satish and H. G. Shivakumar, 2006, Hydrogels as Controlled Drug Delivery Systems: Synthesis, Crosslinking, Water and Drug Transport Mechanism, **Indian J Pharm Sci,** 68(2), 133-140.

Schacht, E. H., 2004, Polymer chemistry and hydrogel systems, **Journal of Physics: Conference,** 3, 22–28.

Shargel, L. and A. B. C. Yu, 1999, **Applied Biopharmaceutics and Pharmacokinetics**, 4th ed., McGraw-Hill, New York, 132-147.

Singhal, P., K. Kumar, M. Pandey, and S. A. Saraf, 2010, Evaluation of Acyclovir Loaded Oil Entrapped Calcium alginate Beads Prepared by Ionotropic Gelation Method, **International Journal of ChemTech Research,** 2(4), 2076-2085.

Sinha, V. R., A.K. Singla, S. Wadhawan, R. Kaushik, R. Kumria, K. Bansal and S. Dhawan, 2004, Chitosan Microspheres as a Potential Carrier for Drugs, **International Journal of Pharmaceutics,** 274, 1–33.

Slaughter, B. V., S. S. Khurshid, O. Z. Fisher, A. Khademhosseini and N. A. Peppas, 2009, Hydrogels in Regenerative Medicine, **Adv. Mater.,** 21, 3307–3329.

Sudipto, K. D., N. R. Aluru, B. Johnson, W. C. Crone, D. J. Beebe and J. Moore, 2002, **Journal of Microelectromechanical Systems,** 11(5), 544-554.

Sweetman, S. C., 2009, **Martindale The Complete Drug Reference**, 36th ed., Pharmaceutical Press, London, 44, 2141, 2370.

Takahashi, M., N. Umehara and M. Tezuka, 2001, Persistent Analgesic Effect of Sustained Release Diclofenac Sodium Preparation on Bovine Type II Collagen-Induced Arthritis, **Journal of Health Science,** 48(1), 48–54.

United States Pharmacopeial Convention, 2006, **The United States Pharmacopeia**, 29th ed., **The National Formulary**, 24th rev., United States Pharmacopeial Convention Inc., Rockville, 732.

United States Pharmacopeial Convention, 2007, **The United States Pharmacopeia**, 30th ed., **The National Formulary**, 25th rev., United States Pharmacopeial Convention Inc., Rockville, 751.

Wagner, J. G. and M. Pernarowski, 1971, **Biopharmaceutics and Relevant Pharmacokinetics**, 1st ed., Drug Intelligence Publications, Hamilton, Illinois, 98-99, 104-105, 115-116.

Wang, Q., J. Zhang and A. Wang, 2009, Preparation and Characterization of a Novel pH-Sensitive Chitosan-g-Poly (acrylic acid) / Attapulgite / Sodium Alginate Composite Hydrogel Bead for Controlled Release of Diclofenac Sodium, **Carbohydrate Polymers,** 78, 731-737.

Wicaksono, Y., 2006, Pengembangan Sediaan Lepas Lambat Na Diklofenak Berbasis Matrik Etilselulosa – PVP K 30, **Jurnal Ilmu Dasar,** 7(2), 170-176.

Zarzycki, R., Z. Modrzejewska1 and K. Nawrotek1, 2010, Drug Release From Hydrogel Matrices, **Ecological Chemistry And Engineering S,** 17(2), 117-135.

Zulkarnain, A. K., T. Yuwono dan Sumarno, 2001, Preformulasi Sediaan Lepas Lambat Natrium Diklofenak Dengan Resin Penukar Ion, **Majalah Farmasi Indonesia,** 12(1), 20-27.

LAMPIRAN A

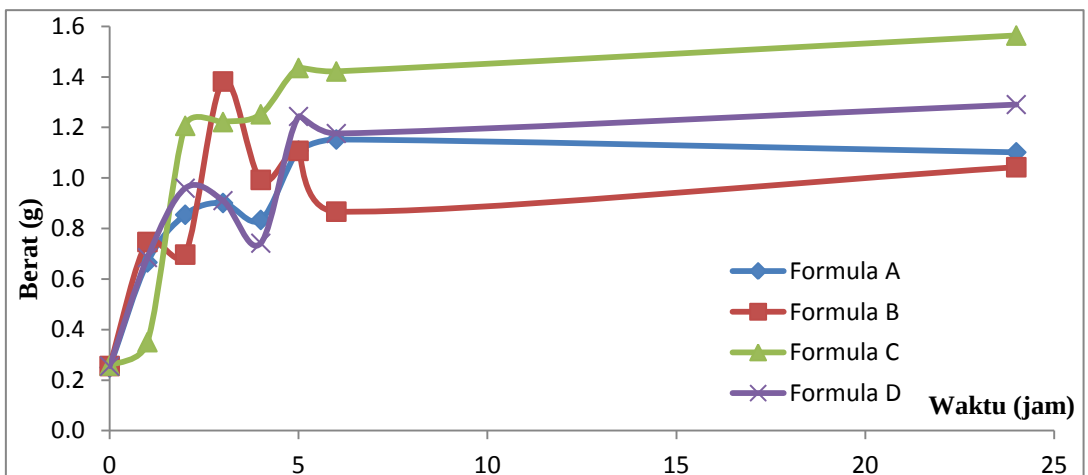
PENGEMBANGAN

1. Pengembangan hidrogel dalam dapar pH 2,1 (replikasi I)

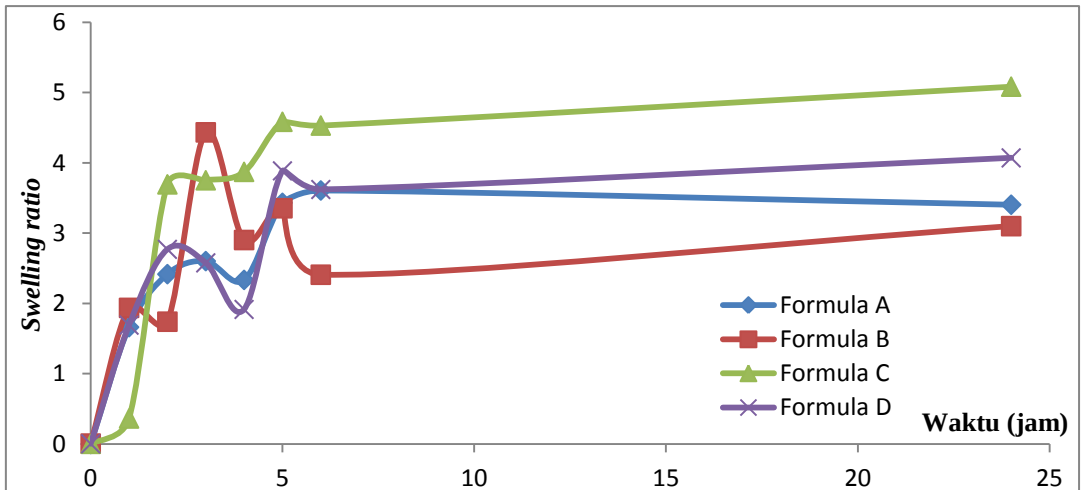
Waktu (jam)	Evaluasi berat hidrogel (gram)				*Swelling Ratio* / SR			
	Formula A	Formula B	Formula C	Formula D	Formula A	Formula B	Formula C	Formula D
0	0,2502	0,2560	0,2578	0,2544	0,0004	0,0067	0,0031	0,0035
1	0,6660	0,7469	0,3505	0,6851	1,6629	1,9371	0,3638	1,6919
2	0,8547	0,6970	1,2066	0,9596	2,4174	1,7409	3,6949	2,7705
3	0,9012	1,3821	1,2216	0,9106	2,6034	4,4349	3,7533	2,5780
4	0,8342	0,9926	1,2524	0,7420	2,3355	2.9033	3,8732	1,9155
5	1,1085	1,1076	1,4355	1,2438	3,4322	3,3555	4,5856	3,8872
6	1,1525	0,8670	1,4217	1,1763	3,6082	2,4094	4,5319	3,6620
24	1,1018	1,0428	1,5640	1,2908	3,4054	3,1007	5,0856	4,0719
$\bar{x} \pm$ SD	0,8586 ± 0,2970	0,8865 ± 0,3346	1,0888 ± 0,5001	0,9080 ± 0,3458	2,4332 ± 1,1877	2,4860 ± 1,3156	3,2364 ± 1,9459	2,5676 ± 1,3588

2. Pengurangan volume dari pengembangan hidrogel dalam dapar pH 2,1 (replikasi I)

Volume	Formula A (mL)	Formula B (mL)	Formula C (mL)	Formula D (mL)
Awal	50	50	50	50
Akhir	43	45	42,5	44



3. Gambar pengembangan hidrogel dalam dapar pH 2,1 (replikasi I)



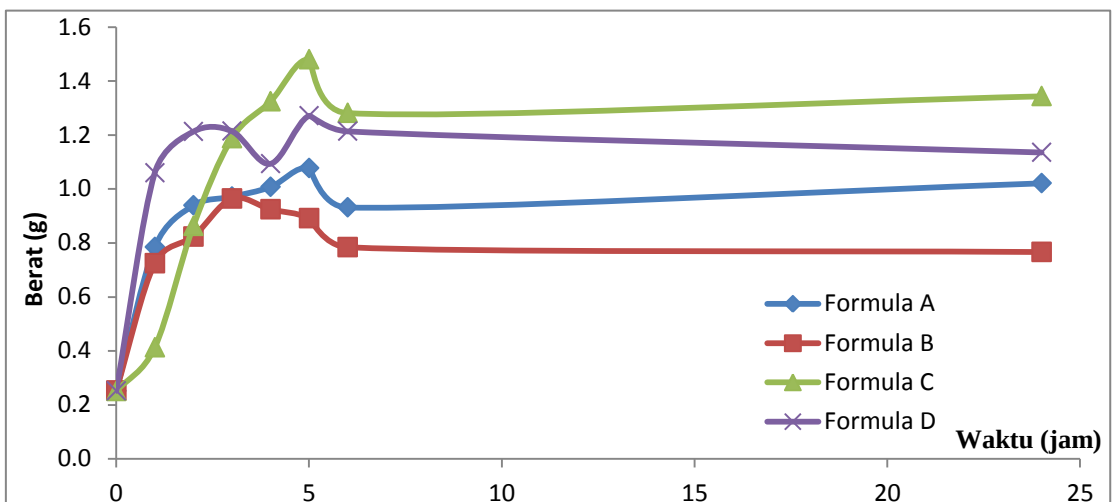
4. Gambar *swelling ratio* / rasio pengembangan dalam dapar pH 2,1 (replikasi I)

5. Pengembangan hidrogel dalam dapar pH 2,1 (replikasi II)

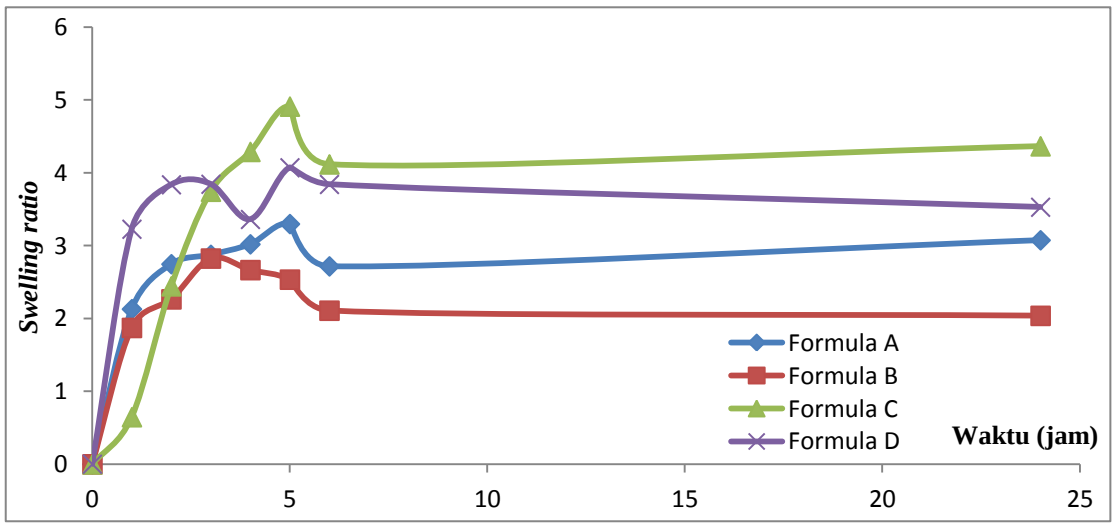
Waktu (jam)	Evaluasi berat hidrogel (gram)				*Swelling Ratio*/SR			
	Formula A	Formula B	Formula C	Formula D	Formula A	Formula B	Formula C	Formula D
0	0,2514	0,2527	0,2508	0,2506	0,0036	0,0028	0,0016	0,0040
1	0,7846	0,7244	0,4130	1,0597	2,1321	1,8746	0,6494	3,2287
2	0,9391	0,8232	0,8628	1,2127	2,7489	2,2667	2,4457	3,8392
3	0,9714	0,9643	1,1879	1,2144	2,8778	2,8266	3,7440	3,8460
4	1,0076	0,9244	1,3247	1,0934	3,0224	2,6683	4,2903	3,3631
5	1,0772	0,8914	1,4804	1,2713	3,3002	2,5373	4,9121	4,0730
6	0,9317	0,7840	1,2818	1,2137	2,7194	2,1111	4,1190	3,8432
24	1,0214	0,7662	1,3440	1,1354	3,0774	2,0405	4,3674	3,5307
$\bar{x} \pm$ SD	0,8731 ± 0,2655	0,7663 ± 0,2233	1,0182 ± 0,4616	1,0565 ± 0,3329	2,4852 ± 1,0600	2,0410 ± 0,8860	3,0662 ± 1,8433	3,2160 ± 1,3283

6. Pengurangan volume dari pengembangan hidrogel dalam dapar pH 2,1 (replikasi II)

Volume	Formula A (mL)	Formula B (mL)	Formula C (mL)	Formula D (mL)
Awal	50	50	50	50
Akhir	45	45	44,5	45,5



7. Gambar pengembangan hidrogel dalam dapar pH 2,1 (replikasi II)



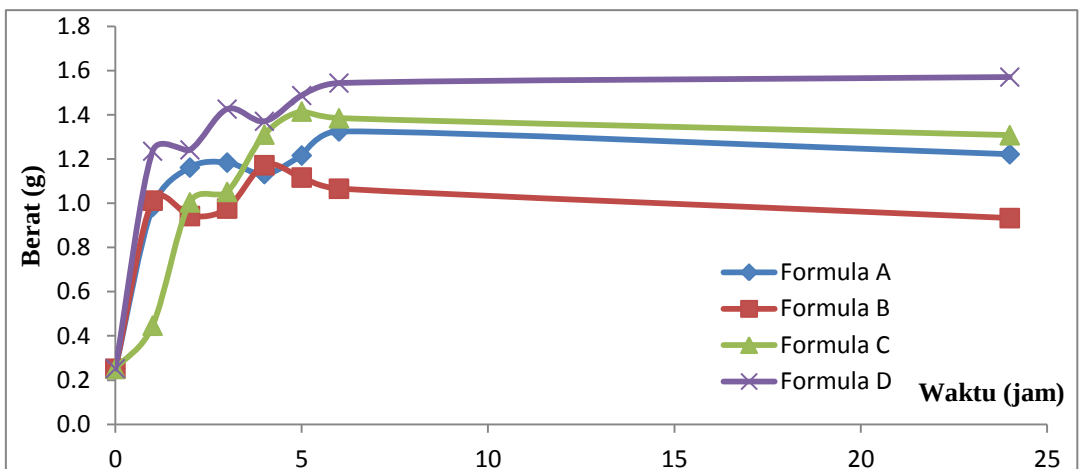
8. Gambar *swelling ratio* / rasio pengembangan dalam dapar pH 2,1 (replikasi II)

9. Pengembangan dari hidrogel dalam dapar pH 2,1 (replikasi III)

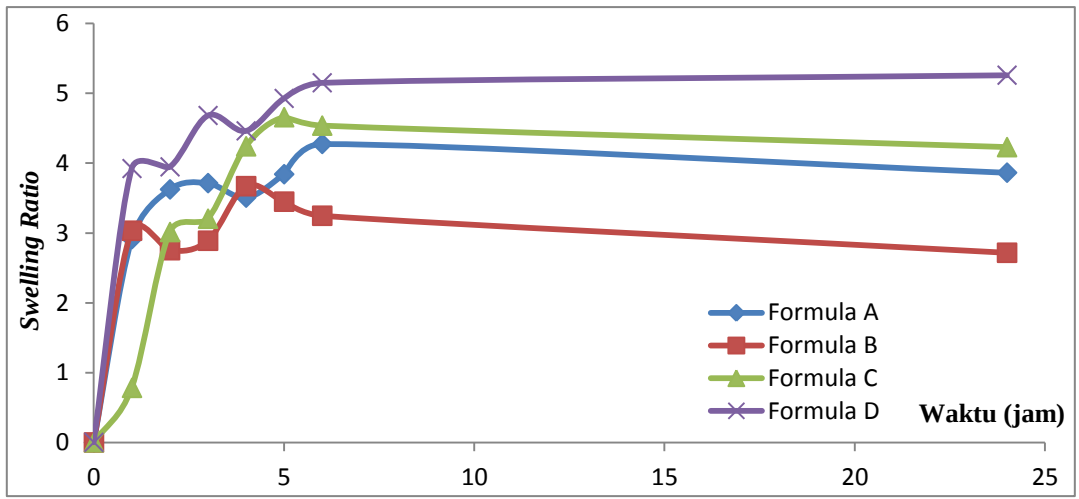
Waktu (jam)	Evaluasi berat hidrogel (gram)				*Swelling Ratio*/SR			
	Formula A	Formula B	Formula C	Formula D	Formula A	Formula B	Formula C	Formula D
0	0,2517	0,2516	0,2511	0,2521	0,0020	0,0024	0,0040	0,0044
1	0,9830	1,0121	0,4462	1,2355	2,9132	3,0323	0,7841	3,9223
2	1,1616	0,9423	1,0039	1,2416	3,6242	2,7542	3,0140	3,9466
3	1,1841	0,9762	1,0515	1,4261	3,7138	2,8892	3,2043	4,6817
4	1,1320	1,1721	1,3107	1,3709	3,5064	3,6697	4,2407	4,4618
5	1,2161	1,1165	1,4149	1,4874	3,8412	3,4482	4,6573	4,9259
6	1,3250	1,0659	1,3847	1,5437	4,2747	3,2466	4,5366	5,1502
24	1,2217	0,9330	1,3078	1,5709	3,8635	2,7171	4,2291	5,2586
$\bar{x} \pm$ SD	1,0594 ± 0,3404	0,9337 ± 0,2881	1,0214 ± 0,4437	1,2660 ± 0,4285	3,2174 ± 1,3549	2,7200 ± 1,1478	3,0838 ± 1,7740	4,0439 ± 1,7072

10. Pengurangan volume dari pengembangan hidrogel dalam dapar pH 2,1 (replikasi III)

Volume	Formula A (mL)	Formula B (mL)	Formula C (mL)	Formula D (mL)
Awal	50	50	50	50
Akhir	42	43	44	43,5



11. Gambar pengembangan hidrogel dalam dapar pH 2,1 (replikasi III)



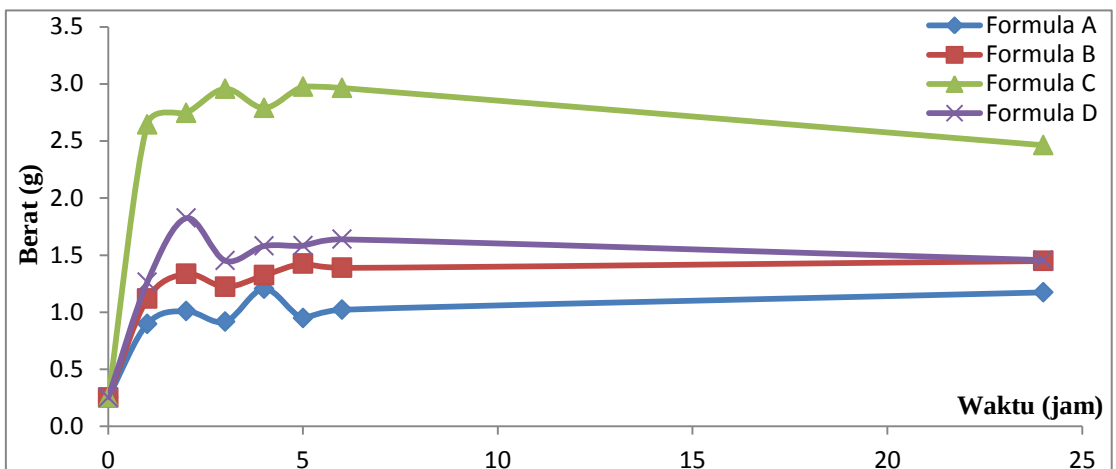
12. Gambar *swelling ratio* / rasio pengembangan dalam dapar pH 2,1 (replikasi III)

13. Pengembangan dari hidrogel dalam dapar pH 7,4 (replikasi I)

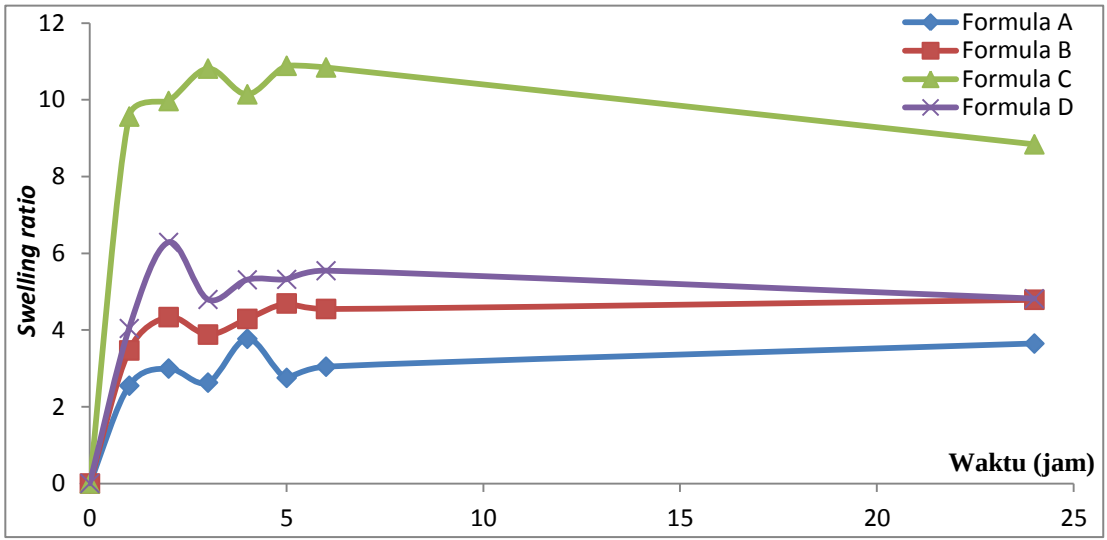
Waktu (jam)	Evaluasi berat hidrogel (gram)				*Swelling Ratio*/SR			
	Formula A	Formula B	Formula C	Formula D	Formula A	Formula B	Formula C	Formula D
0	0,2526	0,2507	0,2510	0,2514	0,0012	0,0020	0,0028	0,0040
1	0,8958	1,1184	2,6445	1,2626	2,5505	3,4700	9,5653	4,0423
2	1,0086	1,3356	2,7457	1,8247	2,9976	4,3381	9,9696	6,2871
3	0,9161	1,2219	2,9574	1,4518	2,6310	3,8837	10,8154	4,7979
4	1,2042	1,3239	2,7897	1,5802	3,7729	4,2914	10,1454	5,3107
5	0,9474	1,4248	2,9757	1,5831	2,7551	4,6946	10,8885	5,3223
6	1,0209	1,3888	2,9649	1,6394	3,0464	4,5508	10,8454	5,5471
24	1,1731	1,4487	2,4634	1,4569	3,6496	4,7902	8,8418	4,8183
$\bar{x} \pm$ SD	0,9273 ± 0,2950	1,1891 ± 0,3944	2,4740 ± 0,9158	1,3813 ± 0,4848	2,6755 ± 1,1693	3,7526 ± 1,5765	8,8843 ± 3,6588	4,5162 ± 1,9359

14. Pengurangan volume dari pengembangan hidrogel dalam dapar pH 7,4 (replikasi I)

Volume	Formula A (mL)	Formula B (mL)	Formula C (mL)	Formula D (mL)
Awal	50	50	50	50
Akhir	42	42,5	41	43



15. Gambar pengembangan hidrogel dalam dapar pH 7,4 (replikasi I)



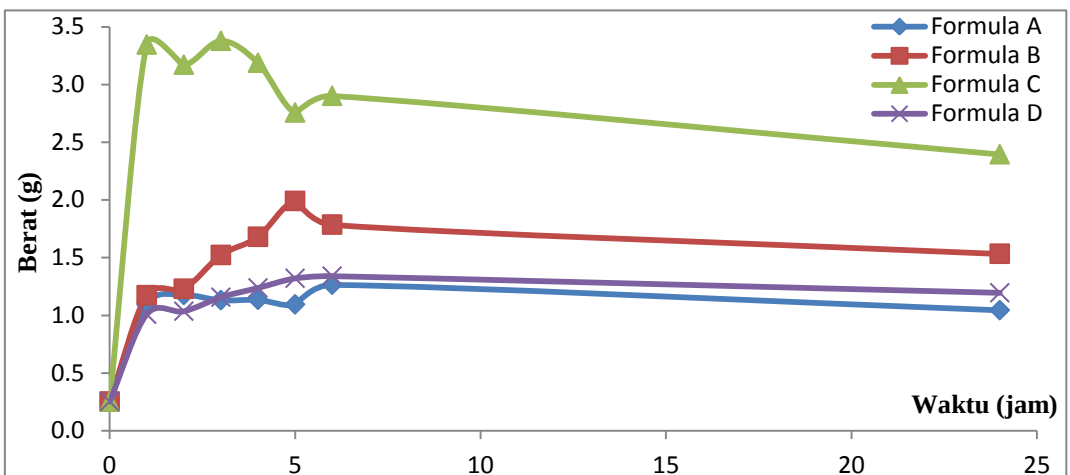
16. Gambar *swelling ratio* / rasio pengembangan dalam dapar pH 7,4 (replikasi I)

17. Pengembangan dari hidrogel dalam dapar pH 7,4 (replikasi II)

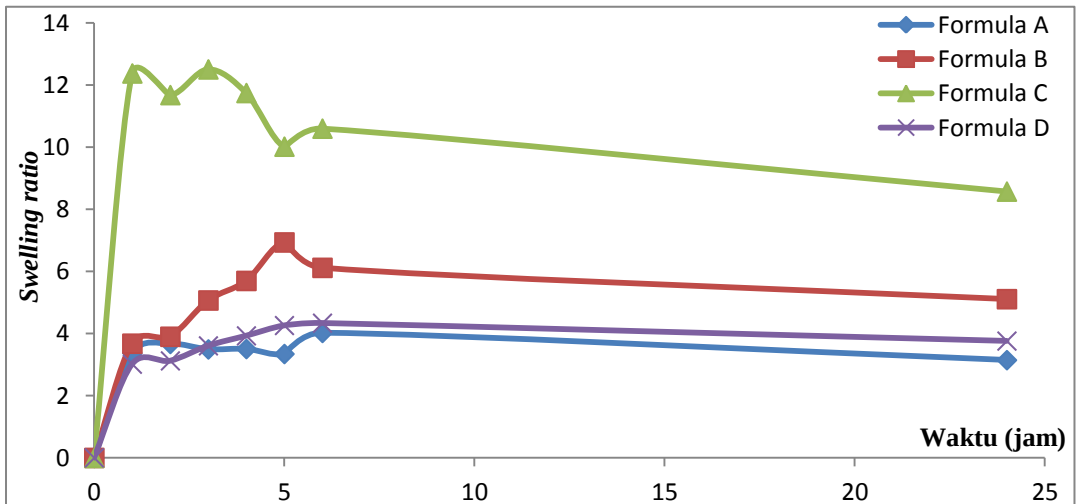
Waktu (jam)	Evaluasi berat hidrogel (gram)				*Swelling Ratio*/SR			
	Formula A	Formula B	Formula C	Formula D	Formula A	Formula B	Formula C	Formula D
0	0,2520	0,2517	0,2509	0,2518	0,0020	0,0040	0,0032	0,0044
1	1,0995	1,1731	3,3456	1,0075	3,3718	3,6793	12,3770	3,0187
2	1,1750	1,2290	3,1715	1,0344	3,6720	3,9023	11,6809	3,1260
3	1,1306	1,5219	3,3783	1,1558	3,4954	5,0706	12,5078	3,6103
4	1,1336	1,6796	3,1881	1,2367	3,5074	5,6996	11,7473	3,9330
5	1,0934	1,9901	2,7565	1,3197	3,3475	6,9382	10,0216	4,2641
6	1,2641	1,7852	2,9013	1,3389	4,0262	6,1209	10,6006	4,3406
24	1,0436	1,5324	2,3948	1,1944	3,1495	5,1125	8,5754	3,7643
$\bar{x} \pm$ SD	1,0240 ± 0,3186	1,3954 ± 0,5354	2,6734 ± 1,0328	1,0674 ± 0,3505	3,0715 ± 1,2669	4,5659 ± 2,1355	9,6892 ± 4,1295	3,2577 ± 1,3980

18. Pengurangan volume dari pengembangan hidrogel dalam dapar pH 7,4 (replikasi II)

Volume	Formula A (mL)	Formula B (mL)	Formula C (mL)	Formula D (mL)
Awal	50	50	50	50
Akhir	42	42,5	42	43,5



19. Gambar pengembangan hidrogel dalam dapar pH 7,4 (replikasi II)



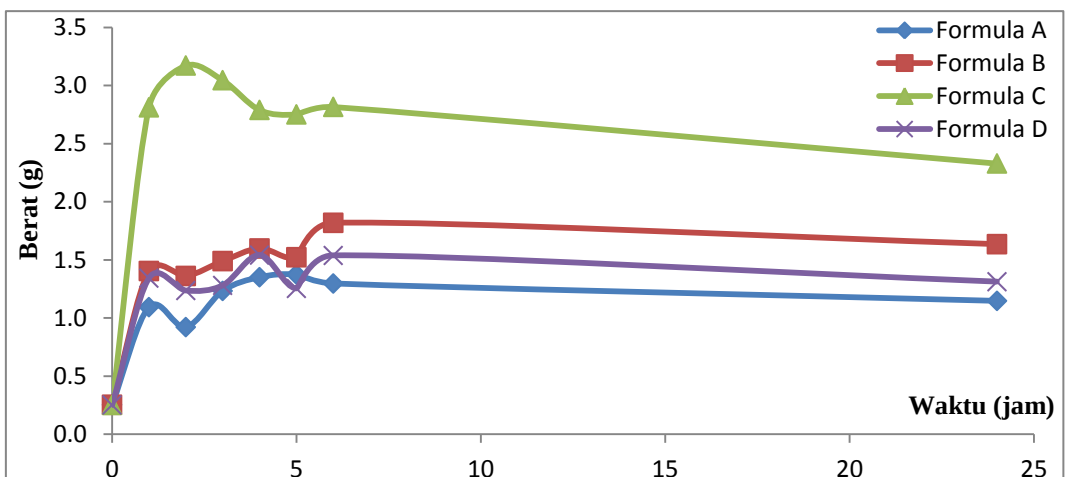
20. Gambar *swelling ratio* / rasio pengembangan dalam dapar pH 7,4 (replikasi II)

21. Pengembangan dari hidrogel dalam pH 7,4 (replikasi III)

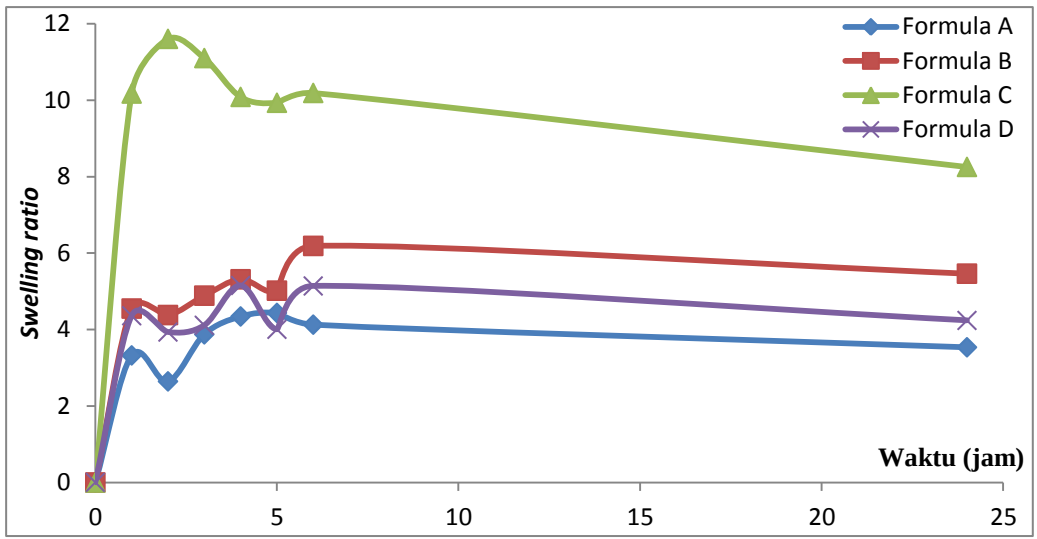
Waktu (jam)	Evaluasi berat hidrogel (gram)				*Swelling Ratio*/SR			
	Formula A	Formula B	Formula C	Formula D	Formula A	Formula B	Formula C	Formula D
0	0,2532	0,2535	0,2519	0,2514	0,0016	0,0020	0,0008	0,0040
1	1,0934	1,4043	2,8128	1,3428	3,3252	4,5506	10,1752	4,3626
2	0,9216	1,3614	3,1727	1,2360	2,6456	4,3810	11,6051	3,9361
3	1,2328	1,4897	3,0462	1,2801	3,8766	4,8881	11,1025	4,1122
4	1,3509	1,5980	2,7905	1,5409	4,3438	5,3162	10,0866	5,1538
5	1,3742	1,5227	2,7519	1,2538	4,4359	5,0186	9,9333	4,0072
6	1,2968	1,8189	2,8166	1,5379	4,1297	6,1893	10,1903	5,1418
24	1,1472	1,6352	2,3296	1,3121	3,5380	5,4632	8,2555	4,2400
$\bar{x} \pm$ SD	1,0838 ± 0,3671	1,3855 ± 0,4792	2,4965 ± 0,9396	1,2194 ± 0,4090	3,2870 ± 1,4523	4,4761 ± 1,8940	8,9187 ± 3,7329	3,8697 ± 1,6333

22. Pengurangan volume dari pengembangan hidrogel dalam dapar pH 7,4 (replikasi III)

Volume	Formula A (mL)	Formula B (mL)	Formula C (mL)	Formula D (mL)
Awal	50	50	50	50
Akhir	42	44	43	44



23. Gambar pengembangan hidrogel dalam dapar pH 7,4 (replikasi III)



24. Gambar *swelling ratio* / rasio pengembangan dalam dapar pH 7,4 (replikasi III)

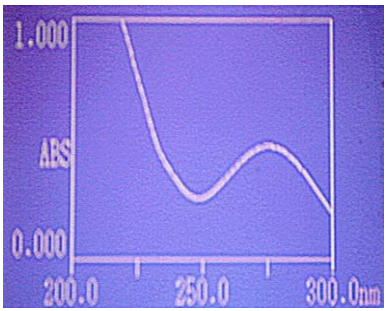
LAMPIRAN B

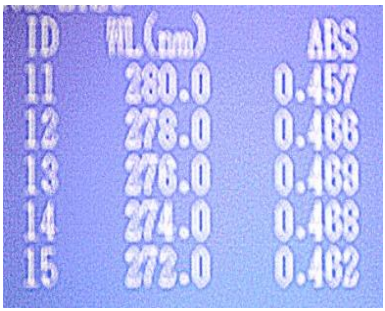
HASIL VALIDASI PENETAPAN KADAR NATRIUM DIKLOFENAK SECARA SPEKTROFOTOMETER

Hasil pembuatan larutan baku induk dan linearitas natrium diklofenak

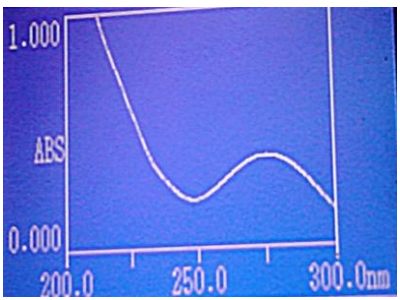
a. Penentuan panjang gelombang maksimum

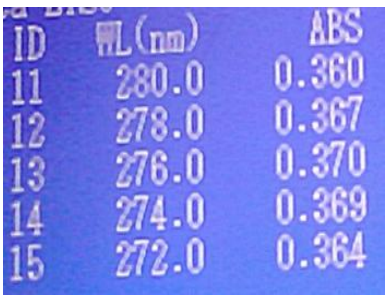
Panjang gelombang maksimum ditentukan dengan menggunakan larutan baku kerja natrium diklofenak dalam aquades pada konsentrasi 14 µg/mL dan diperoleh panjang gelombang maksimum 276 nm.



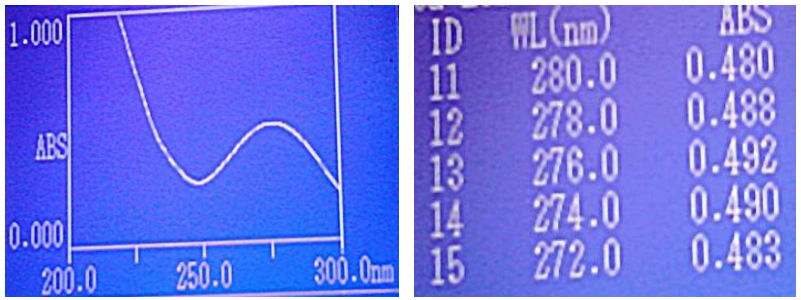


25. Gambar pemilihan panjang gelombang serapan maksimum dalam aquades pada konsentrasi 14 µg/mL (replikasi I)





26. Gambar pemilihan panjang gelombang serapan maksimum dalam aquades pada konsentrasi 14 µg/mL (replikasi II)



27. Gambar pemilihan panjang gelombang serapan maksimum dalam aquades pada konsentrasi 14 µg/mL (replikasi III)

b. <u>Pembuatan larutan baku induk natrium diklofenak dan linearitas dalam aquades</u>

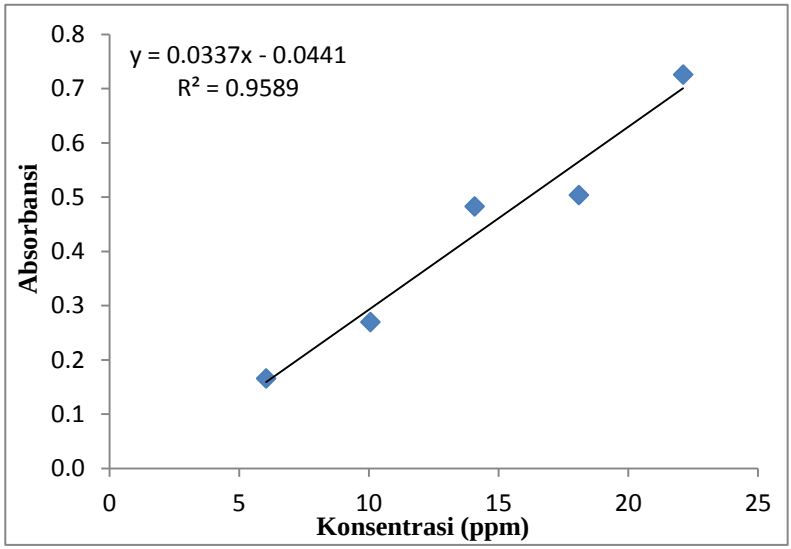
Pada pembuatan larutan baku induk replikasi I sejumlah berat natrium diklofenak yang ditimbang adalah 0,1005 g (100,5 mg) dan kemudian dilarutkan hingga 100 mL dengan aquades dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi I) yang didapat adalah $\frac{100{,}5\ mg}{100\ mL}$ = 1005 µg/mL (1005 ppm).

Pada pembuatan larutan baku induk replikasi II sejumlah berat natrium diklofenak yang ditimbang adalah 0,1013 g (101,3 mg) dan kemudian dilarutkan hingga 100 mL dengan aquades dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi II) yang didapat adalah = $\frac{101{,}3\ mg}{100\ mL}$ = 1013 µg/mL (1013 ppm).

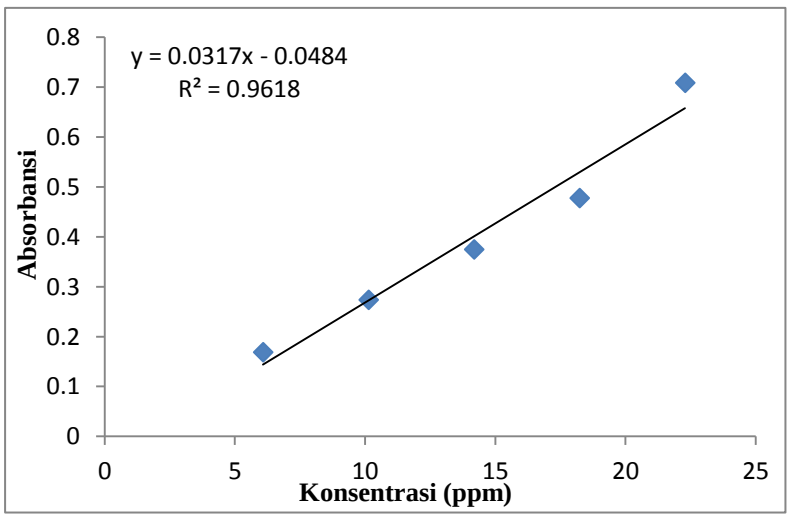
Pada pembuatan larutan baku induk replikasi III sejumlah berat natrium diklofenak yang ditimbang adalah 0,1001 g (100,1 mg) dan kemudian dilarutkan hingga 100 mL dengan aquades dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi III) yang didapat adalah = $\frac{100{,}1\ mg}{100\ mL}$ = 1001 µg/mL (1001 ppm).

28. Tabel linearitas dari kurva baku induk dalam aquades

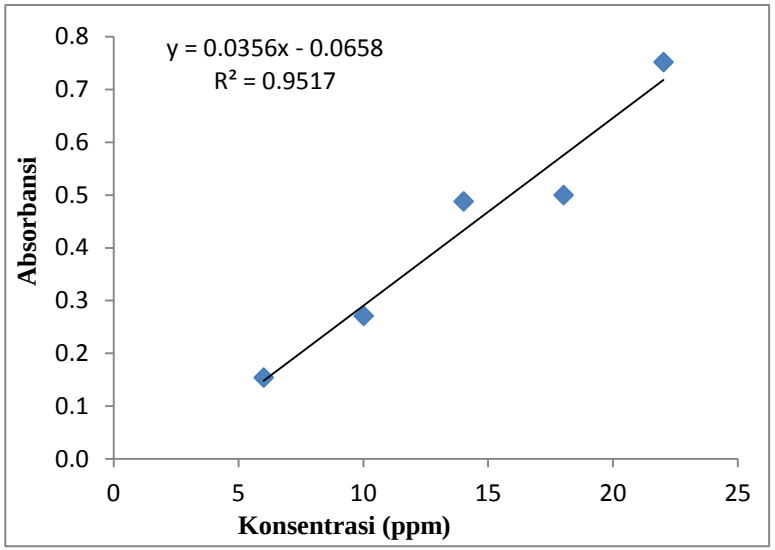
Repli-kasi	Konsen-trasi	Linearitas	Absor-bansi
I	C1	$\frac{0{,}06\ mL}{10\ mL} \times 1005$ = 6,03 ppm	0,166
	C2	$\frac{0{,}10\ mL}{10\ mL} \times 1005$ = 10,05 ppm	0,270
	C3	$\frac{0{,}14\ mL}{10\ mL} \times 1005$ = 14,07 ppm	0,483
	C4	$\frac{0{,}18\ mL}{10\ mL} \times 1005$ = 18,09 ppm	0,504
	C5	$\frac{0{,}22\ mL}{10\ mL} \times 1005$ = 22,11 ppm	0,726
II	C1	$\frac{0{,}06\ mL}{10\ mL} \times 1013$ = 6,078 ppm	0,169
	C2	$\frac{0{,}10\ mL}{10\ mL} \times 1013$ = 10,13 ppm	0,274
	C3	$\frac{0{,}14\ mL}{10\ mL} \times 1013$ = 14,182 ppm	0,375
	C4	$\frac{0{,}18\ mL}{10\ mL} \times 1013$ = 18,234 ppm	0,478
	C5	$\frac{0{,}22\ mL}{10\ mL} \times 1013$ = 22,286 ppm	0,709
III	C1	$\frac{0{,}06\ mL}{10\ mL} \times 1001$ = 6,006 ppm	0,154
	C2	$\frac{0{,}10\ mL}{10\ mL} \times 1001$ = 10,01 ppm	0,271
	C3	$\frac{0{,}14\ mL}{10\ mL} \times 1001$ = 14,014 ppm	0,488
	C4	$\frac{0{,}18\ mL}{10\ mL} \times 1001$ = 18,018 ppm	0,500
	C5	$\frac{0{,}22\ mL}{10\ mL} \times 1001$ = 22,022 ppm	0,752



29. Gambar kurva linearitas dalam aquades replikasi I



30. Gambar kurva linearitas dalam aquades replikasi II



31. Gambar kurva linearitas dalam aquades replikasi III

Harga koefisien korelasi yang diperoleh $\geq$ 0,95 dimana r hitung > r tabel (0,878), maka dipilih harga koefisien korelasi yang paling besar. Harga intersep harus $\leq$ 2% dari serapan pada kadar konsentrasi terkecil dalam rentang kurva baku sehingga dipilih harga intersep yang paling kecil dan nilai *slope* antara ketiga persamaan diatas harus tidak ada perbedaan yang bermakna (F hitung < F tabel) sehingga salah satu persamaan yang dapat digunakan adalah y = 0,0337x - 0,0441.

32. Hasil penetapan kadar hidrogel natrium diklofenak

Replikasi	Formula	Absorbansi	C sampel (µg/ml)	C teoritis (µg/ml)	Kadar (%)
I	A	0,280	9,6172	68,69436	114,4906
	B	0,297	10,1217	72,29758	120,496
	C	0,247	8,6380	61,69987	102,8331
	D	0,254	8,8457	63,18355	105,3059
II	A	0,291	9,9436	71,02586	118,3764
	B	0,312	10,5668	75,47690	125,7948
	C	0,239	8,4006	60,00424	100,0071
	D	0,249	8,6973	62,12378	103,5396
III	A	0,285	9,7656	69,75413	116,2569
	B	0,289	9,8843	70,60195	117,6699
	C	0,252	8,7864	62,75964	104,5994
	D	0,261	9,0534	64,66723	107,7787

Contoh perhitungan akurasi dan presisi :

%	Bahan aktif (mg)	Matriks (mg)	+ aquades ad (mL)	Pipet (mL)	+ aquades ad (mL)	Konsentrasi (ppm)
100	100	1500	100	0,14	10	14

Absorbansi = 0,436 $\longrightarrow$ y = 0,0337x - 0,0441

Konsentrasi sebenarnya = 14,2364

Konsentrasi teoritis = 14,0280

$$\% \text{ perolehan kembali} = \frac{\text{konsentrasi sebenarnya}}{\text{konsentrasi teoritis}} \times 100\ \%$$

$$= \frac{14,2364}{14,028} \times 100\ \% = 101,4856\ \%$$

$$\text{Untuk menghitung \% KV} = \frac{SD}{\bar{x}} \times 100\%$$

$$= \frac{2,0012}{101,7689} \times 100\ \% = 1,9664\%$$

LAMPIRAN C

LOADING OBAT DAN EFISIENSI ENKAPSULASI

33. Hasil *loading* obat dan efisiensi enkapsulasi

Repli-kasi	Formula	Absorbansi	FP	C ppm	Wt	Dosis-Wt	*Loading* obat (%)	Efisiensi enkapsulasi (%)
I	A	0,568	17	323,8615	4,8579	55,1421	55,0320	92,0873
	B	0,613	19	390,8480	5,8627	54,1373	53,8679	90,6799
	C	0,667	12	268,7432	4,0311	55,9689	55,8014	93,5613
	D	0,535	20	358,7162	5,3807	54,6193	54,5647	91,1231
II	A	0,519	18	313,1149	4,6967	55,3033	55,0829	92,5408
	B	0,657	19	419,0912	6,2864	53,7136	53,3933	90,0599
	C	0,654	13	285,4291	4,2814	55,7186	55,5519	93,1429
	D	0,563	20	377,6351	5,6645	54,3355	54,1190	90,9214
III	A	0,556	17	316,9696	4,7545	55,2455	54,9706	92,5361
	B	0,649	19	413,9561	6,2093	53,7907	53,6298	89,9201
	C	0,625	12	251,7162	3,7757	56,2243	56,0003	94,0819
	D	0,543	20	364,1216	5,4618	54,5382	54,3751	91,1697

Contoh perhitungan *loading* obat dan efisiensi enkapsulasi :

Formula	Absorbansi	FP	C ppm	Wt	Dosis-Wt	*Loading* obat (%)	Efisiensi enkapsulasi (%)
A	0,568	17	323,8615	4,8579	55,1421	55,0320	92,0873

Absorbansi = 0,568 $\longrightarrow$ 0,0296x + 0,0041

$$\text{Wt} = \frac{\text{C sesungguhnya (µg/mL)}}{1000} \times \text{volume}$$

$$= \frac{323{,}8615}{1000} \times 15 = 4{,}8579 \text{ mg}$$

Dosis - Wt = 60 - 4,8579 = 55,1421 mg

$$\textit{Loading} \text{ obat} = \frac{\text{berat obat dalam hidrogel}}{\text{berat hidrogel}} \times 100\ \% = \frac{55{,}1421 \text{ mg}}{100{,}2 \text{ mg}} \times 100\ \% = 55{,}0321\ \%$$

$$\textit{Loading} \text{ obat teoritis} = \frac{60}{100{,}2} \times 100 = 59{,}8802 \text{ mg}$$

$$\text{Efisiensi enkapsulasi} = \frac{\text{berat obat dalam hidrogel}}{\textit{liading} \text{ obat teoritis}} \times 100\ \% = \frac{55{,}1421 \text{ mg}}{59{,}8802 \text{ mg}} \times 100\ \% = 92{,}0873\ \%$$

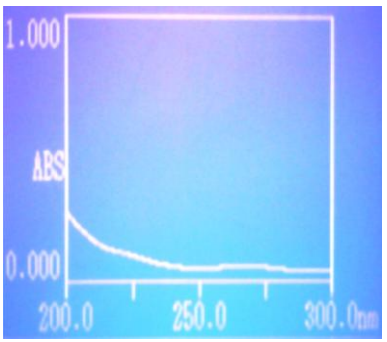
LAMPIRAN D

HASIL VALIDASI PENETAPAN KADAR HASIL DISOLUSI DENGAN MENGGUNAKAN SPEKTROFOTOMETER UV-VIS

Hasil pembuatan larutan baku induk dan linearitas natrium diklofenak

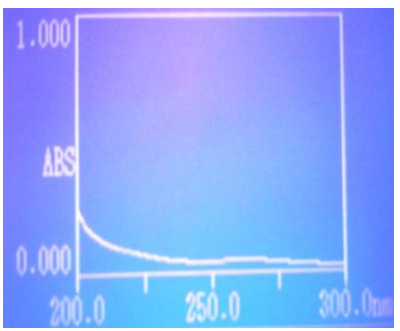
a. Penentuan panjang gelombang maksimum dalam dapar asam klorida pH 2,1

Panjang gelombang maksimum ditentukan dengan menggunakan larutan kerja natrium diklofenak dalam dapar asam klorida pH 2,1 pada konsentrasi 45,5 µg/mL dan diperoleh panjang gelombang maks 264 nm.



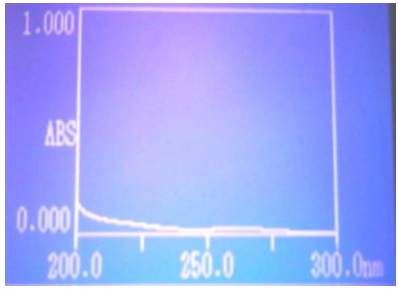
ID	WL(nm)	ABS
16	270.0	0.021
17	268.0	0.023
18	266.0	0.024
19	264.0	0.025
20	262.0	0.025

34. Gambar pemilihan panjang gelombang serapan maksimum dalam dapar pH 2,1 pada konsentrasi 45,5 µg/mL (replikasi I)



ID	WL(nm)	ABS
16	270.0	0.011
17	268.0	0.012
18	266.0	0.013
19	264.0	0.013
20	262.0	0.013

35. Gambar pemilihan panjang gelombang serapan maksimum dalam dapar pH 2,1 pada konsentrasi 45,5 µg/mL (replikasi II)

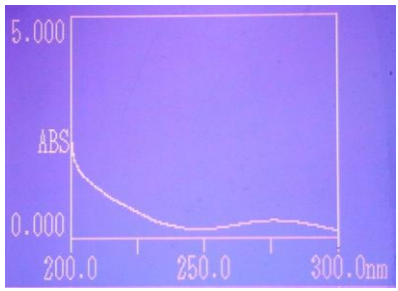


ID	WL(nm)	ABS
16	270.0	0.045
17	268.0	0.046
18	266.0	0.047
19	264.0	0.048
20	262.0	0.048

36. Gambar pemilihan panjang gelombang serapan maksimum dalam dapar pH 2,1 pada konsentrasi 45,5 µg/mL (replikasi III)

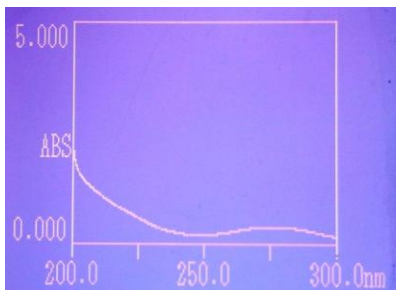
b. <u>Penentuan panjang gelombang maksimum dalam dapar fosfat pH 7,4</u>

Panjang gelombang maksimum ditentukan dengan menggunakan larutan kerja natrium diklofenak dalam dapar fosfat 7,4 pada konsentrasi 14 µg/mL dan diperoleh panjang gelombang maks 276 nm.



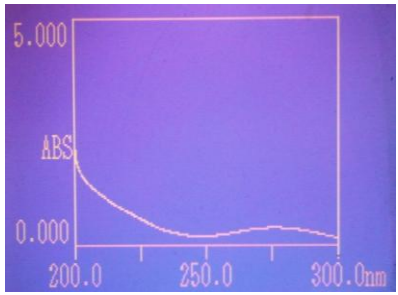
ID	WL(nm)	ABS
11	280.0	0.380
12	278.0	0.385
13	276.0	0.387
14	274.0	0.385
15	272.0	0.378

37. Gambar pemilihan panjang gelombang serapan maksimum dalam dapar pH 7,4 pada konsentrasi 14 µg/mL (replikasi I)



ID	WL(nm)	ABS
11	280.0	0.378
12	278.0	0.384
13	276.0	0.386
14	274.0	0.384
15	272.0	0.377

38. Gambar pemilihan panjang gelombang serapan maksimum dalam dapar pH 7,4 pada konsentrasi 14 µg/mL (replikasi II)



ID	WL(nm)	ABS
11	280.0	0.381
12	278.0	0.388
13	276.0	0.390
14	274.0	0.388
15	272.0	0.382

39. Gambar pemilihan panjang gelombang serapan maksimum dalam dapar pH 7,4 pada konsentrasi 14 µg/mL (replikasi III)

c. <u>Pembuatan larutan baku induk natrium diklofenak dan linearitas dalam dapar pH 2,1</u>

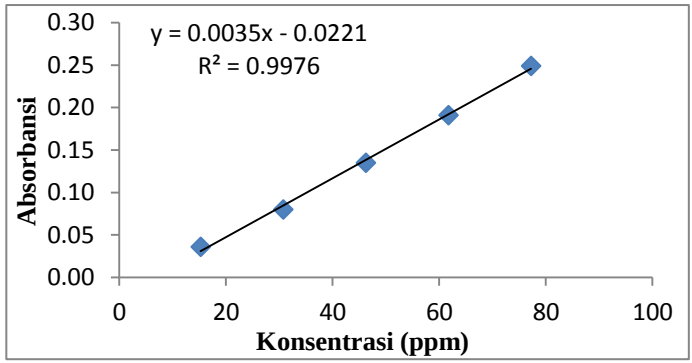
Pada pembuatan larutan baku induk replikasi I sejumlah berat natrium diklofenak yang ditimbang adalah 0,0122 g (12,2mg) dan kemudian dilarutkan hingga 100 mL dengan dapar pH 2,1 dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi I) yang didapat adalah $\frac{12{,}2\ mg}{100\ mL}$ = 122 µg/mL (122 ppm).

Pada pembuatan larutan baku induk replikasi II sejumlah berat natrium diklofenak yang ditimbang adalah 0,0123 g (12,3 mg) dan kemudian dilarutkan hingga 100 mL dengan dapar pH 2,1 dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi II) yang didapat adalah $\frac{12{,}3\ mg}{100\ mL}$ = 123 µg/mL (123 ppm).

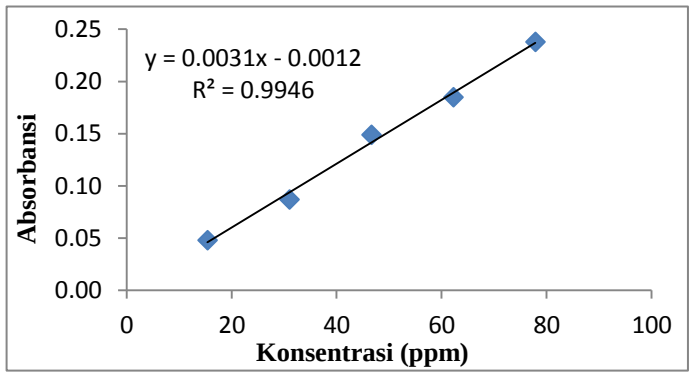
Pada pembuatan larutan baku induk replikasi III sejumlah berat natrium diklofenak yang ditimbang adalah 0,0122 g (12,2 mg) dan kemudian dilarutkan hingga 100 mL dengan dapar pH 2,1 dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi III) yang didapat adalah $\frac{12{,}2\ mg}{100\ mL}$ = 122 µg/mL (122 ppm).

40. Tabel linearitas dari kurva baku induk dalam dapar pH 2,1

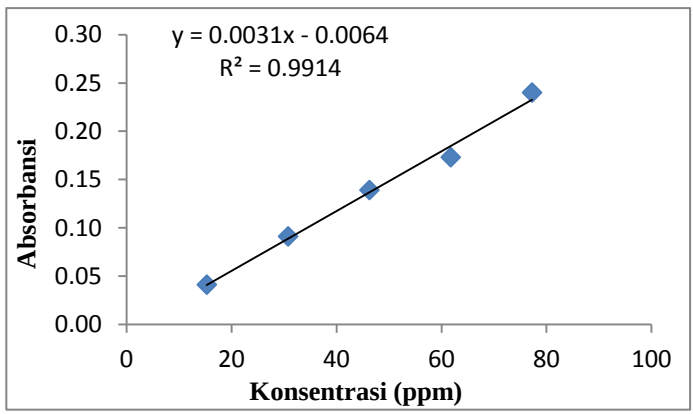
Repli-kasi	Konsen-trasi	Linearitas	Absor-bansi
I	C1	$\frac{1{,}25\ mL}{10\ mL} \times 122$ = 15,25 ppm	0,036
	C2	$\frac{2{,}52\ mL}{10\ mL} \times 122$ = 30,744 ppm	0,080
	C3	$\frac{3{,}79\ mL}{10\ mL} \times 122$ = 46,238 ppm	0,135
	C4	$\frac{5{,}06\ mL}{10\ mL} \times 122$ = 61,732 ppm	0,191
	C5	$\frac{6{,}33\ mL}{10\ mL} \times 122$ = 77,226 ppm	0,249
II	C1	$\frac{1{,}25\ mL}{10\ mL} \times 123$ = 15,375 ppm	0,048
	C2	$\frac{2{,}52\ mL}{10\ mL} \times 123$ = 30,996 ppm	0,087
	C3	$\frac{3{,}79\ mL}{10\ mL} \times 123$ = 46,617 ppm	0,149
	C4	$\frac{5{,}06\ mL}{10\ mL} \times 123$ = 62,238 ppm	0,185
	C5	$\frac{6{,}33\ mL}{10\ mL} \times 123$ = 77,859 ppm	0,238
III	C1	$\frac{1{,}25\ mL}{10\ mL} \times 122$ = 15,25 ppm	0,041
	C2	$\frac{2{,}52\ mL}{10\ mL} \times 122$ = 30,744 ppm	0,091
	C3	$\frac{3{,}79\ mL}{10\ mL} \times 122$ = 46,238 ppm	0,139
	C4	$\frac{5{,}06\ mL}{10\ mL} \times 122$ = 61,732 ppm	0,173
	C5	$\frac{6{,}33\ mL}{10\ mL} \times 122$ = 77,226 ppm	0,240



41. Gambar kurva linearitas dalam dapar pH 2,1 replikasi I



42. Gambar kurva linearitas dalam dapar pH 2,1 replikasi II



43. Gambar kurva linearitas dalam dapar pH 2,1 replikasi III

Harga koefisien korelasi yang diperoleh ≥ 0,99 dimana r hitung > r tabel (0,878), maka dipilih harga koefisien korelasi yang paling besar. Harga intersep harus ≤ 2% dari serapan pada kadar konsentrasi terkecil dalam rentang kurva baku sehingga dipilih harga intersep yang paling kecil dan nilai *slope* antara ketiga persamaan diatas harus tidak ada perbedaan yang bermakna (F hitung < F tabel) sehingga salah satu persamaan yang dapat digunakan adalah y = 0,0031x - 0,0012.

d. Pembuatan larutan baku induk natrium diklofenak dan linearitas dalam dapar pH 7,4

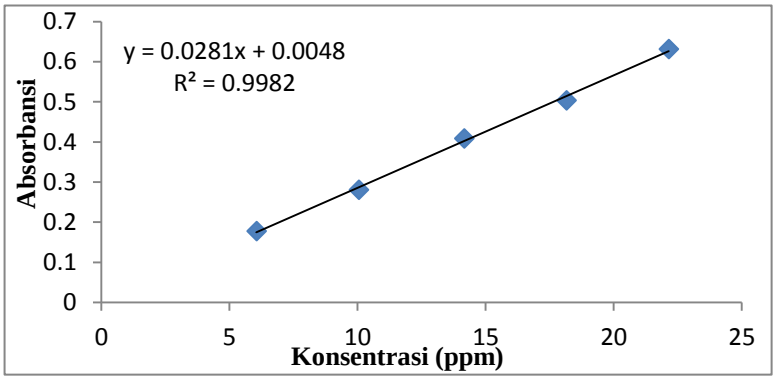
Pada pembuatan larutan baku induk replikasi I sejumlah berat natrium diklofenak yang ditimbang adalah 0,0121 g (12,1 mg) dan kemudian dilarutkan hingga 100 mL dengan dapar pH 7,4 dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi I) yang didapat adalah $\frac{12{,}1\ mg}{100\ mL}$ = 121 µg/mL (121 ppm).

Pada pembuatan larutan baku induk replikasi II sejumlah berat natrium diklofenak yang ditimbang adalah 0,0123 g (12,3 mg) dan kemudian dilarutkan hingga 100 mL dengan dapar pH 7,4 dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi II) yang didapat adalah $\frac{12{,}3\ mg}{100\ mL}$ = 123 µg/mL (123 ppm).

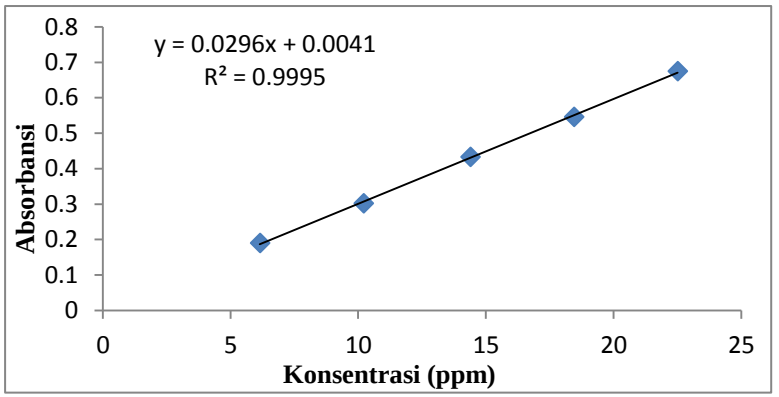
Pada pembuatan larutan baku induk replikasi III sejumlah berat natrium diklofenak yang ditimbang adalah 0,0122 g (12,2 mg) dan kemudian dilarutkan hingga 100 mL dengan dapar pH 7,4 dalam labu 100 mL. Sehingga konsentrasi natrium diklofenak (C baku induk replikasi III) yang didapat adalah $\frac{12{,}2\ mg}{100\ mL}$ = 122 µg/mL (122 ppm).

44. Tabel linearitas dari kurva baku induk dalam dapar pH 7,4

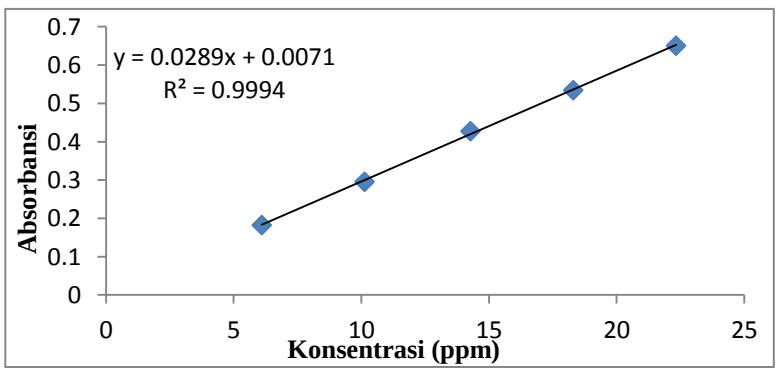
Repli-kasi	Konsen-trasi	Linearitas	Absor-bansi
I	C1	$\frac{0{,}5\ mL}{10\ mL} \times 121 =$ 6,05 ppm	0,178
	C2	$\frac{0{,}83\ mL}{10\ mL} \times 121 =$ 10,043 ppm	0,281
	C3	$\frac{1{,}17\ mL}{10\ mL} \times 121 =$ 14,157 ppm	0,409
	C4	$\frac{1{,}5\ mL}{10\ mL} \times 121 =$ 18,15 ppm	0,504
	C5	$\frac{1{,}83\ mL}{10\ mL} \times 121 =$ 22,143 ppm	0,632
II	C1	$\frac{0{,}5\ mL}{10\ mL} \times 123 =$ 6,15 ppm	0,190
	C2	$\frac{0{,}83\ mL}{10\ mL} \times 123 =$ 10,209 ppm	0,302
	C3	$\frac{1{,}17\ mL}{10\ mL} \times 123 =$ 14,391 ppm	0,433
	C4	$\frac{1{,}5\ mL}{10\ mL} \times 123 =$ 18,45 ppm	0,546
	C5	$\frac{1{,}83\ mL}{10\ mL} \times 123 =$ 22,509 ppm	0,675
III	C1	$\frac{0{,}5\ mL}{10\ mL} \times 122 =$ 6,1 ppm	0,183
	C2	$\frac{0{,}83\ mL}{10\ mL} \times 122 =$ 10,126 ppm	0,296
	C3	$\frac{1{,}17\ mL}{10\ mL} \times 122 =$ 14,274 ppm	0,428
	C4	$\frac{1{,}5\ mL}{10\ mL} \times 122 =$ 18,3 ppm	0,535
	C5	$\frac{1{,}83\ mL}{10\ mL} \times 122 =$ 22,326 ppm	0,651



45. Gambar kurva linearitas dalam dapar pH 7,4 replikasi I



46. Gambar kurva linearitas dalam dapar pH 7,4 replikasi II



47. Gambar kurva linearitas dalam dapar pH 7,4 replikasi III

Harga koefisien korelasi yang diperoleh $\geq$ 0,99 dimana r hitung > r tabel (0,878), maka dipilih harga koefisien korelasi yang paling besar. Harga intersep harus $\leq$ 2% dari serapan pada kadar konsentrasi terkecil dalam rentang kurva baku sehingga dipilih harga intersep yang paling kecil dan nilai *slope* antara ketiga persamaan diatas harus tidak ada perbedaan yang bermakna (F hitung < F tabel) sehingga salah satu persamaan yang dapat digunakan adalah y = 0,0296x + 0,0041.

Contoh pehitungan Wt :

t (menit)	Abs	FP	C ppm	Wt	Wt~ - Wt	Dosis - Wt	%Wt percobaan	%Wt dosis	AUC
30	0,052	-	17,1613	8,5806	19,5161	51,4194	30,5396	14,3011	128,7097
60	0,082	-	26,8387	13,4194	14,6774	46,5806	47,7612	22,3656	330,0000

$$Wt = \frac{\text{C sesungguhnya } (\mu g/mL)}{1000} \times \text{volume medium disolusi}$$

Untuk formula A replikasi I pada t=30 menit

$$Wt = \frac{17,1613}{1000} \times 500$$

Wt = 8,5806 mg

Contoh perhitungan AUC :

Pada formula A replikasi 1,

Untuk t = 30 menit, AUC $= \frac{1}{2} \times Wt \times t_1$

$= \frac{1}{2} \times 8,5806 \times 30$

$= 128,7097$

Untuk t = 60 menit dan seterusnya, AUC $= \frac{1}{2} \times (Wt_n + Wt_{n-1}) \times (t_n - t_{n-1})$

$= \frac{1}{2} \times (13,4194 + 8,5806) \times (60 - 30)$

$= 330,0000$

Luas □ = tlast x berat obat

= 480 x 60

= 28800

$\%ED = \frac{\text{AUC total}}{\text{luas } \square} \times 100\ \%$

$= \frac{9360,9677}{28800} \times 100\ \% = 32,5034\ \%$

LAMPIRAN E

HASIL UJI STATISTIK BERDASARKAN *DESIGN EXPERT*

48. Hasil uji statistik pengembangan hidrogel dalam dapar pH 7,4

Use your mouse to right click on individual cells for definitions.

Response 1 Pengembangan 7,4

ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	2.83	3	0.94	107.32	< 0.0001	significant
A-Chitosan	*0.84*	*1*	*0.84*	*95.26*	*< 0.0001*	
B-Natrium alginat	*0.32*	*1*	*0.32*	*36.84*	*0.0003*	
AB	*1.67*	*1*	*1.67*	*189.86*	*< 0.0001*	
Pure Error	0.070	8	8.796E-003			
Cor Total	2.90	11				

The Model F-value of 107.32 implies the model is significant. There is only
a 0.01% chance that a "Model F-Value" this large could occur due to noise.
Values of "Prob > F" less than 0.0500 indicate model terms are significant.
In this case A, B, AB are significant model terms.
Values greater than 0.1000 indicate the model terms are not significant.
If there are many insignificant model terms (not counting those required to support hierarchy),

model reduction may improve your model.

Std. Dev.	0.094	R-Squared	0.9758
Mean	1.59	Adj R-Squared	0.9667
C.V. %	5.88	Pred R-Squared	0.9454
PRESS	0.16	Adeq Precision	23.539

The "Pred R-Squared" of 0.9454 is in reasonable agreement with the "Adj R-Squared" of 0.9667.

"Adeq Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 23.539 indicates an adequate signal. This model can be used to navigate the design space.

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	1.59	1	0.027	1.53	1.66	
A-*Chitosan*	0.26	1	0.027	0.20	0.33	1.00
B-Natrium alginat	-0.16	1	0.027	-0.23	-0.10	1.00
AB	-0.37	1	0.027	-0.44	-0.31	1.00

Final Equation in Terms of Coded Factors:

Pengembangan 7,4 =

+1.59

+0.26 * A

-0.16 * B

-0.37 * A * B

Final Equation in Terms of Actual Factors:

Pengembangan 7,4 =
+1.59428
+0.26425 * *Chitosan*
-0.16433 * Natrium alginat
-0.37307 * *Chitosan* * Natrium alginat

The Diagnostics Case Statistics Report has been moved to the Diagnostics Node.
In the Diagnostics Node, Select Case Statistics from the View Menu.

Proceed to Diagnostic Plots (the next icon in progression). Be sure to look at the:
1) Normal probability plot of the studentized residuals to check for normality of residuals.
2) Studentized residuals versus predicted values to check for constant error.
3) Externally Studentized Residuals to look for outliers, i.e., influential values.
4) Box-Cox plot for power transformations.

If all the model statistics and diagnostic plots are OK, finish up with the Model Graphs icon.

49. Hasil uji statistik *swelling ratio*/rasio pengembangan dalam dapar pH 7,4

Use your mouse to right click on individual cells for definitions.

Response 2 Swelling ratio 7,4

ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	45.37	3	15.12	110.59	< 0.0001	significant
A-Chitosan	*13.64*	*1*	*13.64*	*99.71*	*< 0.0001*	
B-Natrium alginat	*5.10*	*1*	*5.10*	*37.27*	*0.0003*	
AB	*26.64*	*1*	*26.64*	*194.78*	*< 0.0001*	
Pure Error	1.09	8	0.14			
Cor Total	46.47	11				

The Model F-value of 110.59 implies the model is significant. There is only a 0.01% chance that a "Model F-Value" this large could occur due to noise.

Values of "Prob > F" less than 0.0500 indicate model terms are significant.
In this case A, B, AB are significant model terms.
Values greater than 0.1000 indicate the model terms are not significant.
If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Std. Dev.	0.37	R-Squared	0.9765
Mean	5.35	Adj R-Squared	0.9676
C.V. %	6.91	Pred R-Squared	0.9470
PRESS	2.46	Adeq Precision	23.942

The "Pred R-Squared" of 0.9470 is in reasonable agreement with the "Adj R-Squared" of 0.9676.

"Adeq Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 23.942 indicates an adequate signal. This model can be used to navigate the design space.

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	5.35	1	0.11	5.10	5.60	
A-*Chitosan*	1.07	1	0.11	0.82	1.31	1.00
B-Natrium alginat	-0.65	1	0.11	-0.90	-0.41	1.00
AB	-1.49	1	0.11	-1.74	-1.24	1.00

Final Equation in Terms of Coded Factors:

Swelling ratio 7,4 =

+5.35

+1.07 * A

-0.65 * B

-1.49 * A * B

Final Equation in Terms of Actual Factors:

Swelling ratio 7,4 =

+5.34985

+1.06602 * *Chitosan*

-0.65177 * Natrium alginat

-1.48990 * *Chitosan* * Natrium alginat

The Diagnostics Case Statistics Report has been moved to the Diagnostics Node.
In the Diagnostics Node, Select Case Statistics from the View Menu.

Proceed to Diagnostic Plots (the next icon in progression). Be sure to look at the:
1) Normal probability plot of the studentized residuals to check for normality of residuals.
2) Studentized residuals versus predicted values to check for constant error.
3) Externally Studentized Residuals to look for outliers, i.e., influential values.
4) Box-Cox plot for power transformations.

If all the model statistics and diagnostic plots are OK, finish up with the Model Graphs icon.

50. Hasil uji statistik *loading* obat

Use your mouse to right click on individual cells for definitions.

Response 3 Loading obat

ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F
Model	7.65	3	2.55	63.72	< 0.0001significant
A-Chitosan	*1.64*	*1*	*1.64*	*41.00*	*0.0002*
B-Natrium alginat	*6.01*	*1*	*6.01*	*150.16*	*< 0.0001*
AB	*8.382E-004*	*1*	*8.382E-004*	*0.021*	*0.8885*
Pure Error	0.32	8	0.040		
Cor Total	7.97	11			

The Model F-value of 63.72 implies the model is significant. There is only
a 0.01% chance that a "Model F-Value" this large could occur due to noise.
Values of "Prob > F" less than 0.0500 indicate model terms are significant.
In this case A, B are significant model terms.
Values greater than 0.1000 indicate the model terms are not significant.
If there are many insignificant model terms (not counting those required to support hierarchy),
model reduction may improve your model.

Std. Dev.	0.20	R-Squared	0.9598
Mean	54.70	Adj R-Squared	0.9448
C.V. %	0.37	Pred R-Squared	0.9096
PRESS	0.72	Adeq Precision	18.657

The "Pred R-Squared" of 0.9096 is in reasonable agreement with the "Adj R-Squared" of 0.9448.

"Adeq Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable. Your
ratio of 18.657 indicates an adequate signal. This model can be used to navigate the design space.

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	54.70	1	0.058	54.57	54.83	
A-*Chitosan*	0.37	1	0.058	0.24	0.50	1.00
B-Natrium alginat	-0.71	1	0.058	-0.84	-0.57	1.00
AB	-8.358E-003	1	0.058	-0.14	0.12	1.00

Final Equation in Terms of Coded Factors:

Loading obat =
+54.70
+0.37 * A
-0.71 * B
-8.358E-003 * A * B

Final Equation in Terms of Actual Factors:

Loading obat =
+54.69907
+0.36965 * *Chitosan*
-0.70745 * Natrium alginat
-8.35766E-003 * *Chitosan* * Natrium alginat

The Diagnostics Case Statistics Report has been moved to the Diagnostics Node.
In the Diagnostics Node, Select Case Statistics from the View Menu.

Proceed to Diagnostic Plots (the next icon in progression). Be sure to look at the:

1) Normal probability plot of the studentized residuals to check for normality of residuals.
2) Studentized residuals versus predicted values to check for constant error.
3) Externally Studentized Residuals to look for outliers, i.e., influential values.
4) Box-Cox plot for power transformations.

If all the model statistics and diagnostic plots are OK, finish up with the Model Graphs icon.

51. Hasil uji statistik efisiensi enkapsulasi

Use your mouse to right click on individual cells for definitions.

Response 4 Efisiensi enkapsulasi

ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	19.79	3	6.60	56.11	< 0.0001	significant
A-Chitosan	*3.18*	*1*	*3.18*	*27.04*	*0.0008*	
B-Natrium alginat	*16.51*	*1*	*16.51*	*140.47*	*< 0.0001*	
AB	*0.095*	*1*	*0.095*	*0.81*	*0.3950*	
Pure Error	0.94	8	0.12			
Cor Total	20.73	11				

The Model F-value of 56.11 implies the model is significant. There is only a 0.01% chance that a "Model F-Value" this large could occur due to noise.

Values of "Prob > F" less than 0.0500 indicate model terms are significant.
In this case A, B are significant model terms.
Values greater than 0.1000 indicate the model terms are not significant.
If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Std. Dev.	0.34	R-Squared	0.9546
Mean	91.82	Adj R-Squared	0.9376
C.V. %	0.37	Pred R-Squared	0.8979
PRESS	2.12	Adeq Precision	17.052

The "Pred R-Squared" of 0.8979 is in reasonable agreement with the "Adj R-Squared" of 0.9376.

"Adeq Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 17.052 indicates an adequate signal. This model can be used to navigate the design space.

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	91.82	1	0.099	91.59	92.05	
A-*Chitosan*	0.51	1	0.099	0.29	0.74	1.00
B-Natrium alginat	-1.17	1	0.099	-1.40	-0.94	1.00
AB	-0.089	1	0.099	-0.32	0.14	1.00

Final Equation in Terms of Coded Factors:

Efisiensi enkapsulasi =

+91.82

+0.51 * A

-1.17 * B

-0.089 * A * B

Final Equation in Terms of Actual Factors:
Efisiensi enkapsulasi =
+91.81869
+0.51468 * *Chitosan*
-1.17302 * Natrium alginat
-0.088962 * *Chitosan* * Natrium alginat

The Diagnostics Case Statistics Report has been moved to the Diagnostics Node.
In the Diagnostics Node, Select Case Statistics from the View Menu.

Proceed to Diagnostic Plots (the next icon in progression). Be sure to look at the:
1) Normal probability plot of the studentized residuals to check for normality of residuals.
2) Studentized residuals versus predicted values to check for constant error.
3) Externally Studentized Residuals to look for outliers, i.e., influential values.
4) Box-Cox plot for power transformations.

If all the model statistics and diagnostic plots are OK, finish up with the Model Graphs icon.

52. Hasil uji statistik disolusi dalam dapar pH 7,4

Use your mouse to right click on individual cells for definitions.
Response 5 Disolusi 7,4
ANOVA for selected factorial model
Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	746.33	3	248.78	23.44	0.0003	significant
A-Chitosan	*116.28*	*1*	*116.28*	*10.96*	*0.0107*	
B-Natrium alginat	*11.09*	*1*	*11.09*	*1.04*	*0.3366*	
AB	*618.96*	*1*	*618.96*	*58.33*	*< 0.0001*	
Pure Error	84.90	8	10.61			
Cor Total	831.23	11				

The Model F-value of 23.44 implies the model is significant. There is only a 0.03% chance that a "Model F-Value" this large could occur due to noise.

Values of "Prob > F" less than 0.0500 indicate model terms are significant.
In this case A, AB are significant model terms.
Values greater than 0.1000 indicate the model terms are not significant.
If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Std. Dev.	3.26	R-Squared	0.8979
Mean	57.28	Adj R-Squared	0.8596
C.V. %	5.69	Pred R-Squared	0.7702
PRESS	191.02	Adeq Precision	10.947

The "Pred R-Squared" of 0.7702 is in reasonable agreement with the "Adj R-Squared" of 0.8596.

"Adeq Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 10.947 indicates an adequate signal. This model can be used to navigate the design space.

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	57.28	1	0.94	55.11	59.44	
A-*Chitosan*	-3.11	1	0.94	-5.28	-0.94	1.00
B-Natrium alginat	-0.96	1	0.94	-3.13	1.21	1.00
AB	-7.18	1	0.94	-9.35	-5.01	1.00

Final Equation in Terms of Coded Factors:

Disolusi 7,4 =
+57.28
-3.11 * A
-0.96 * B
-7.18 * A * B

Final Equation in Terms of Actual Factors:

Disolusi 7,4 =
+57.27508
-3.11292 * *Chitosan*
-0.96125 * Natrium alginat
-7.18192 * *Chitosan* * Natrium alginat

The Diagnostics Case Statistics Report has been moved to the Diagnostics Node.
In the Diagnostics Node, Select Case Statistics from the View Menu.

Proceed to Diagnostic Plots (the next icon in progression). Be sure to look at the:

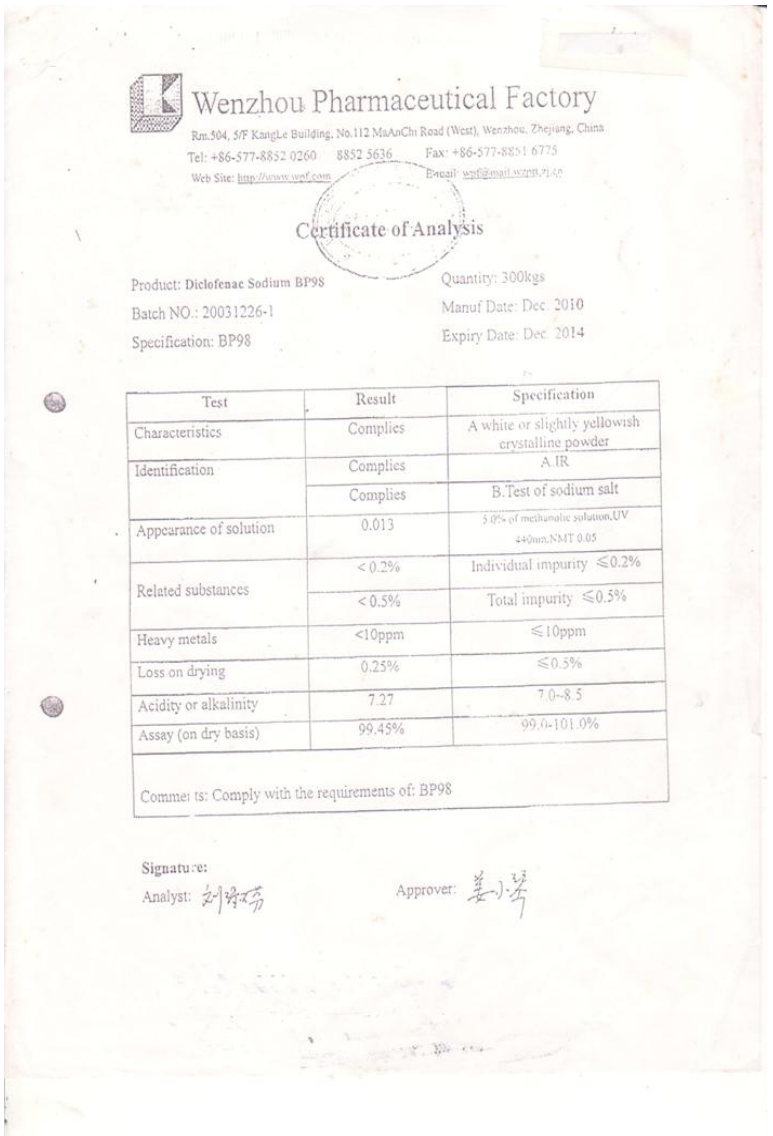
1) Normal probability plot of the studentized residuals to check for normality of residuals.
2) Studentized residuals versus predicted values to check for constant error.
3) Externally Studentized Residuals to look for outliers, i.e., influential values.
4) Box-Cox plot for power transformations.

If all the model statistics and diagnostic plots are OK, finish up with the Model Graphs icon.

LAMPIRAN F

SERTIFIKAT ANALISA

53. Sertifikat analisa bahan natrium diklofenak



Wenzhou Pharmaceutical Factory

Rm.504, 5/F KangLe Building, No.112 MinAnCh Road (West), Wenzhou, Zhejiang, China
Tel: +86-577-8852 0260 8852 5636 Fax: +86-577-8851 6775
Web Site: http://www.wpf.com Email: wpf@mail.wzptt.zj.cn

Certificate of Analysis

Product: Diclofenac Sodium BP98 Quantity: 300kgs
Batch NO.: 20031226-1 Manuf Date: Dec. 2010
Specification: BP98 Expiry Date: Dec. 2014

Test	Result	Specification
Characteristics	Complies	A white or slightly yellowish crystalline powder
Identification	Complies	A.IR
	Complies	B.Test of sodium salt
Appearance of solution	0.013	5.0% of methanolic solution,UV 440nm,NMT 0.05
Related substances	< 0.2%	Individual impurity ≤0.2%
	< 0.5%	Total impurity ≤0.5%
Heavy metals	<10ppm	≤10ppm
Loss on drying	0.25%	≤0.5%
Acidity or alkalinity	7.27	7.0~8.5
Assay (on dry basis)	99.45%	99.0~101.0%
Comments: Comply with the requirements of: BP98		

Signature:
Analyst: Approver:

54. Sertifikat analisa bahan *chitosan*

Laboratorium Bioteknologi Hasper I
Departemen Teknologi Hasil Perairan
Institut Pertanian Bogor

Gedung FPIK Lt.2
Cq: Departemen Teknologi Hasil Perairan
Kampus IPB Darmaga, Bogor 16680

Certificate of Analysis

Product : Chitosan
Date of analysis : December 1, 2011

Parameter	CHITOSAN
Raw material	crab shell
Particle size	Flake or powder (60 mesh)
Water lost on drying (%)/moisture	< 8 %
Ash content (%)	< 0.5 %
Solubility in 1 % acetic acid	> 99 %
Degree of deacetylation	> 80 %
Total Microbial Count	< 10^2 cfu/gram
Coliform	negative
Staphycoccus aureus	negative
Salmonella	negative
Vibrio cholerae	negative
Metals (ppm)	
✓ Pb	< 0.1
✓ Cu	3.38
✓ Zn	3.48
✓ Hg	not detected
✓ As	not detected
✓ Cd	not detected

Head of Laboratory

Linawati Hardjito, PhD

55. Sertifikat analisa bahan natrium alginat

川龙蟒磷制品股份有限公司

Shadong Bio-Technologi
四川龙蟒磷制
Guan zao street 23- block F907
Shanghai china

CERTIFICATE OF ANALYSYS

Product Nama : Sodium Alginate
Other Name : Natii Alginas
Molecular : -
Batch Number : 975-87468-88
Mfg. Date : 01 – 2011
Exp' : 03 – 2014

Identification	Spec	Real
Carateristic	powder	+++
Microbial limit	<200 /g	102 /g
Loss on drying	<15 %	10 %
Sulfated ash	30-36 %	32 %
Ca	<1,5 %	0,9 %
Heavy metal	<20 ppm	9 ppm
Lead	<0,001 %	0,0000045

Adds : High tecnologi development Zone Of Yuncheng, Shandong EP Std

Conclusion : We conform that the goods are complied with EP standard

Corector : 磷制品股份

Approver : 品股份有限公司