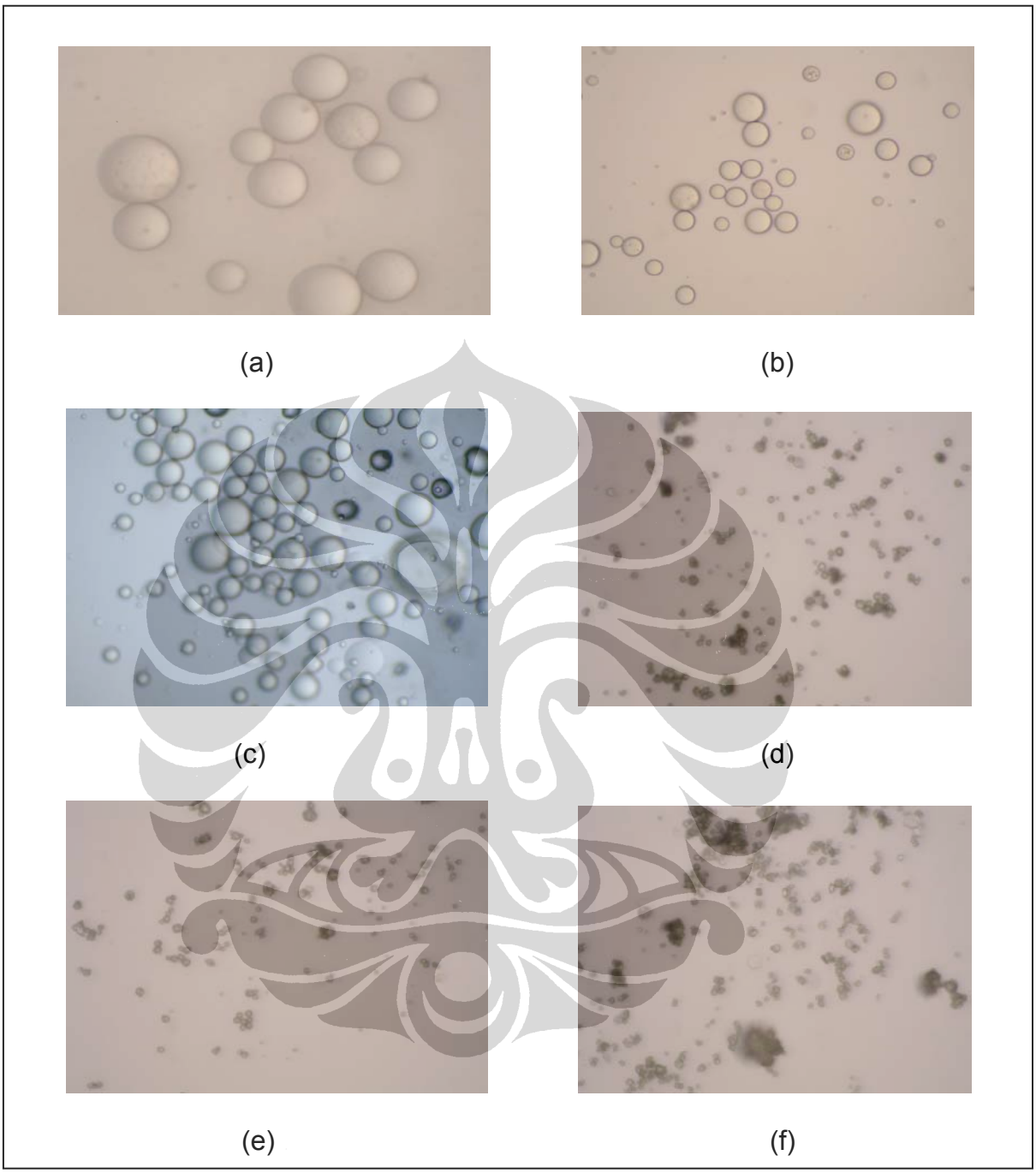
LAMPIRAN

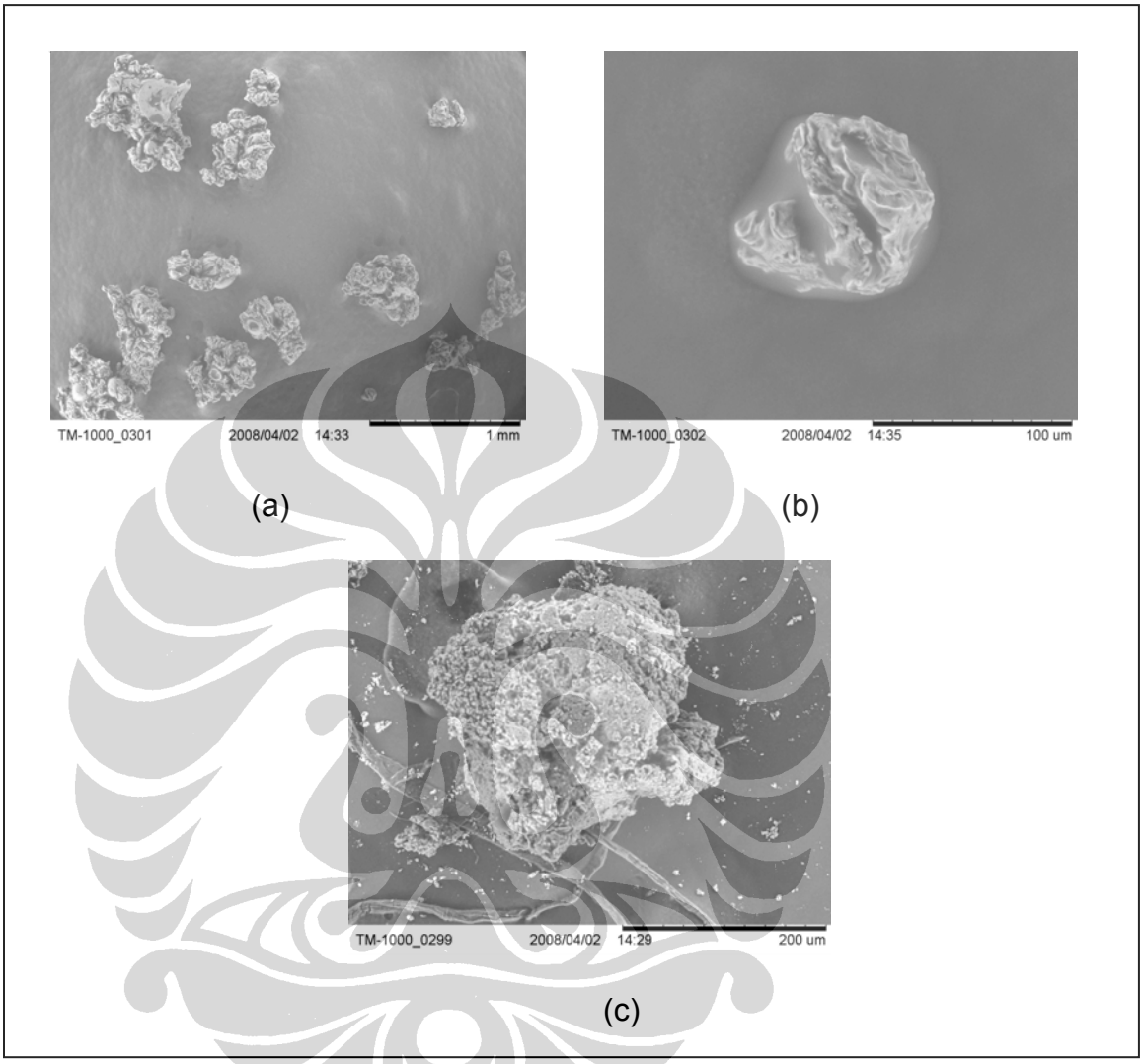
Gambar 4. Alat scanning electron microscopy.

Gambar 5. Alat pengukur distribusi ukuran partikel.

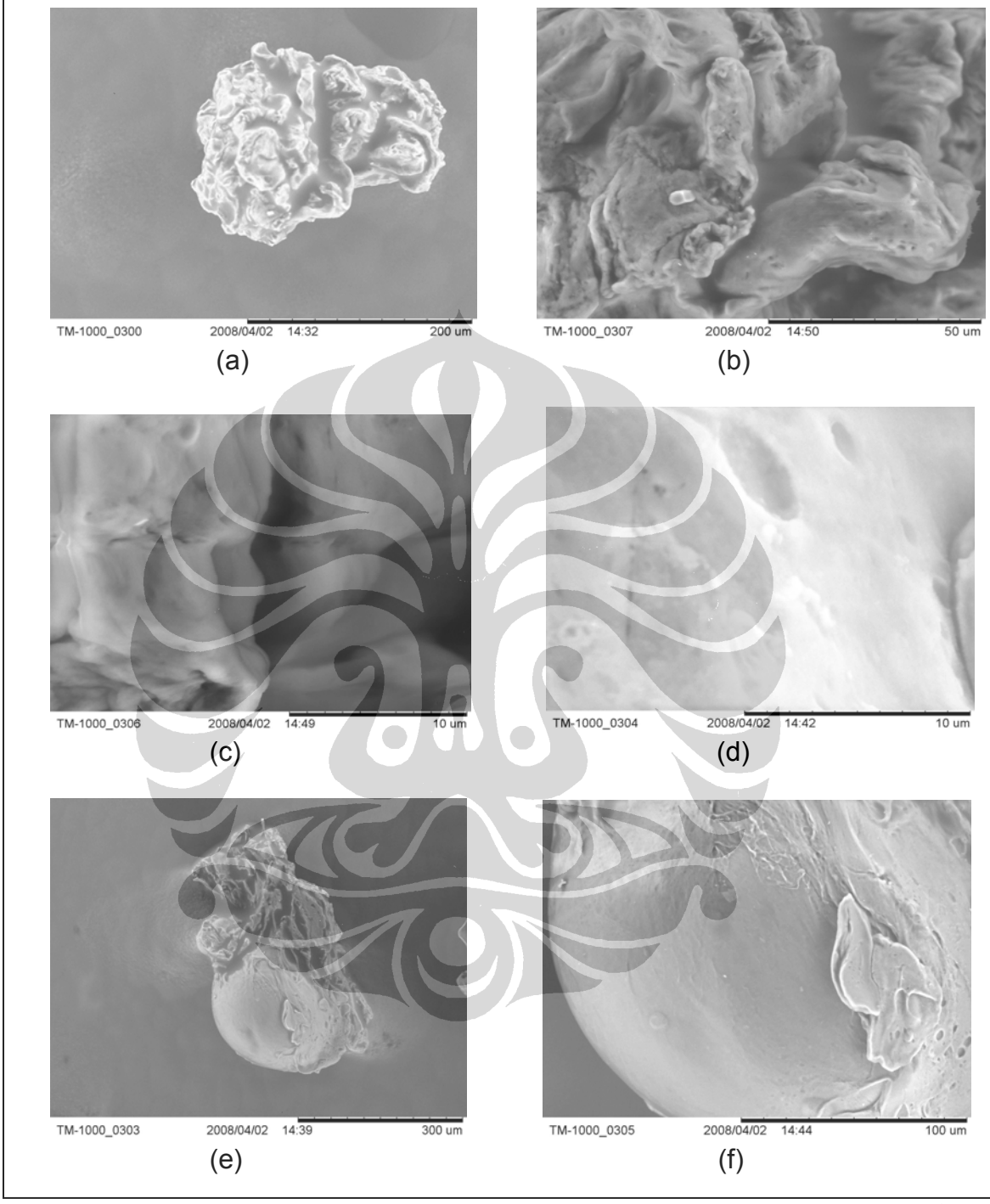
Gambar 6. Alat UV-Vis ELISA reader.



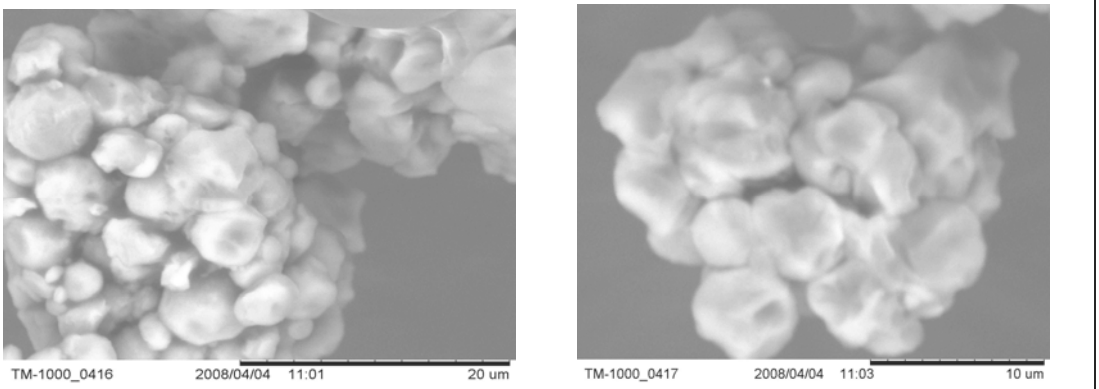
Gambar 7. Mikroskop optik mikrokapsul (perbesaran 100x). (a) emulsi mikrokapsul kosong alginat, (b) emulsi mikrokapsul alginat berisi BSA, (c) emulsi mikrokapsul alginat berisi insulin, (d) mikrokapsul kosong alginat-kitosan, (e) mikrokapsul alginat-kitosan berisi BSA, (f) mikrokapsul alginat-kitosan berisi insulin.



Gambar 8. SEM mikrokapsul kosong alginat. (a) perbesaran 80x, (b) perbesaran 400x, (c) perbesaran 500x.

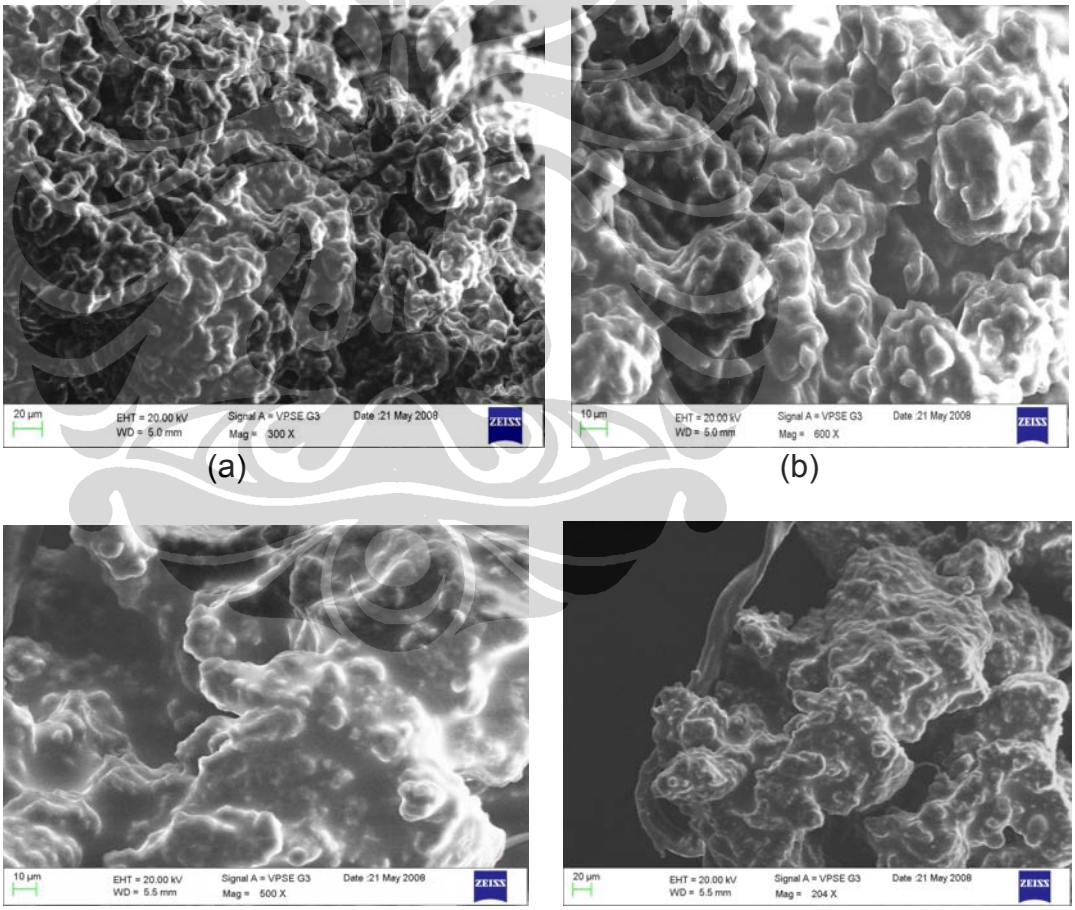


Gambar 9. SEM mikrokapsul alginat berisi protein. (a) perbesaran 800x, (b) perbesaran 1000x, (c) perbesaran 1800x, (d) perbesaran 7000x, (e) perbesaran 250x, (f) perbesaran 1000x.



(a) (b)

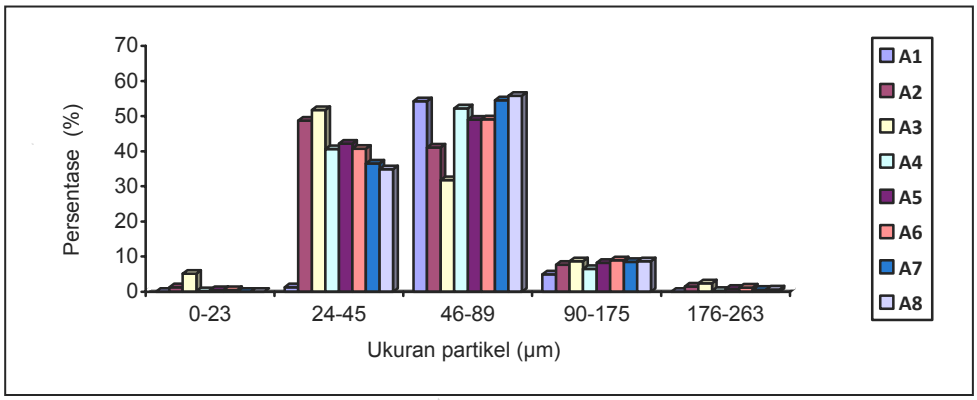
Gambar 10. SEM mikrokapsul alginat berisi protein yang teragregat (perbesaran 5000x).



(a) (b)

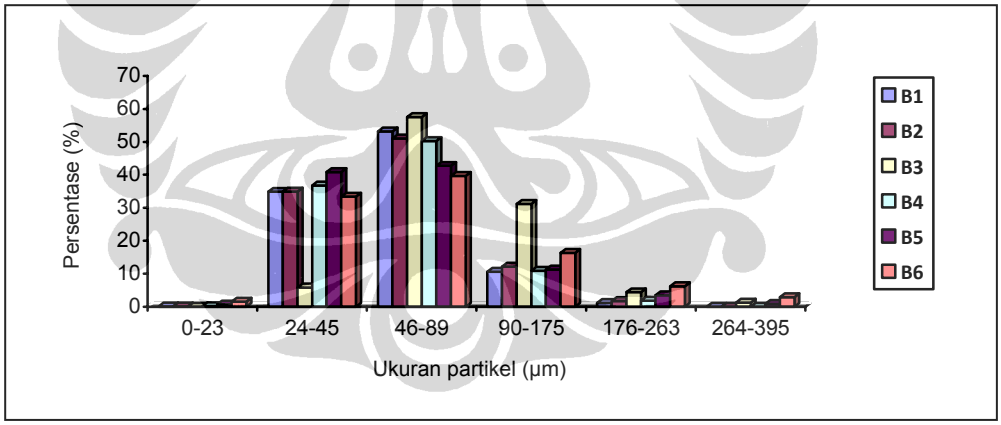
(c) (d)

Gambar 11. SEM mikrokapsul alginat-kitosan. (a) dan (b) mikrokapsul kosong, (c) dan (d) mikrokapsul berisi protein.



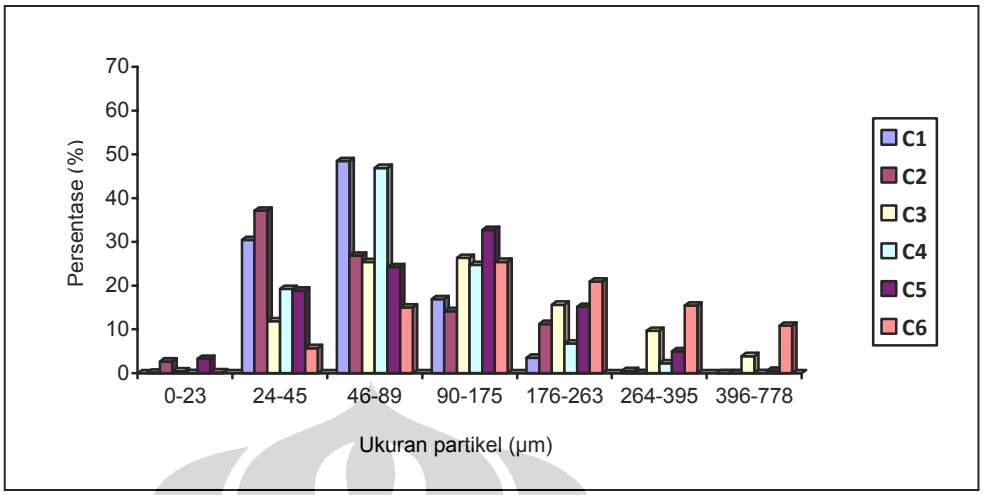
Gambar 12. Distribusi ukuran partikel mikrokapsul alginat.

Keterangan : A1 = mikrokapsul kosong alginat 2%.
A2 = mikrokapsul kosong alginat 3%.
A3 = mikrokapsul kosong alginat 4%.
A4 = mikrokapsul kosong alginat 5%.
A5 = mikrokapsul alginat 2% berisi BSA.
A6 = mikrokapsul alginat 3% berisi BSA.
A7 = mikrokapsul alginat 4% berisi BSA.
A8 = mikrokapsul alginat 5% berisi BSA.



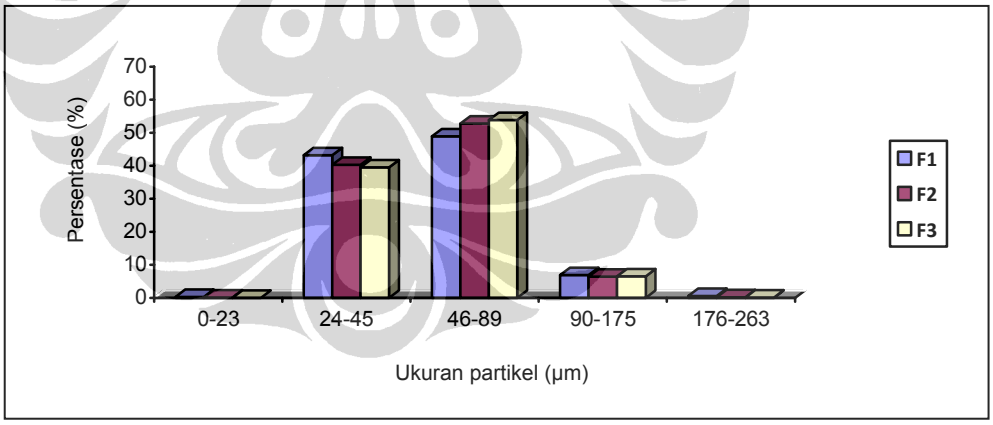
Gambar 13. Distribusi ukuran partikel mikrokapsul alginat 3%-kitosan.

Keterangan : B1 = mikrokapsul kosong alginat 3%-kitosan 0,2%.
B2 = mikrokapsul kosong alginat 3%-kitosan 0,3%.
B3 = mikrokapsul kosong alginat 3%-kitosan 0,4%.
B4 = mikrokapsul alginat 3%-kitosan 0,2% berisi BSA.
B5 = mikrokapsul alginat 3%-kitosan 0,3% berisi BSA.
B6 = mikrokapsul alginat 3%-kitosan 0,4% berisi BSA



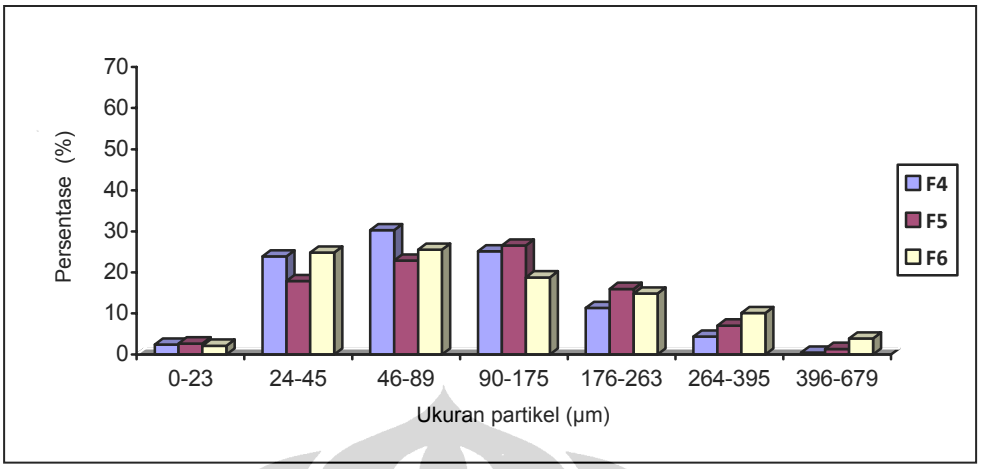
Gambar 14. Distribusi ukuran partikel mikrokapsul alginat 4%-kitosan.

Keterangan : C1 = mikrokapsul kosong alginat 4%-kitosan 0,2%.
C2 = mikrokapsul kosong alginat 4%-kitosan 0,3%.
C3 = mikrokapsul kosong alginat 4%-kitosan 0,4%.
C4 = mikrokapsul alginat 4%-kitosan 0,2% berisi BSA.
C5 = mikrokapsul alginat 4%-kitosan 0,3% berisi BSA.
C6 = mikrokapsul alginat 4%-kitosan 0,4% berisi BSA.



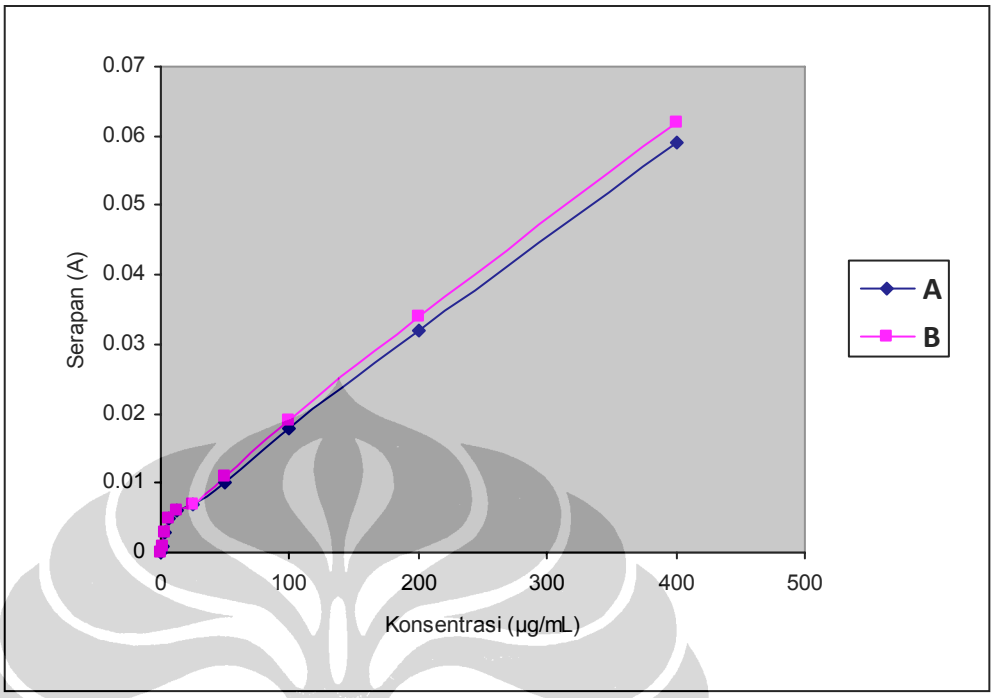
Gambar 15. Distribusi ukuran partikel mikrokapsul alginat 4% berisi insulin.

Keterangan : F1 = mikrokapsul alginat 4% berisi insulin 46,88 IU.
F2 = mikrokapsul alginat 4% berisi insulin 93,75 IU.
F3 = mikrokapsul alginat 4% berisi insulin 187,5 IU.



Gambar 16. Distribusi ukuran partikel mikrokapsul alginat 4%-kitosan 0,3% berisi insulin.

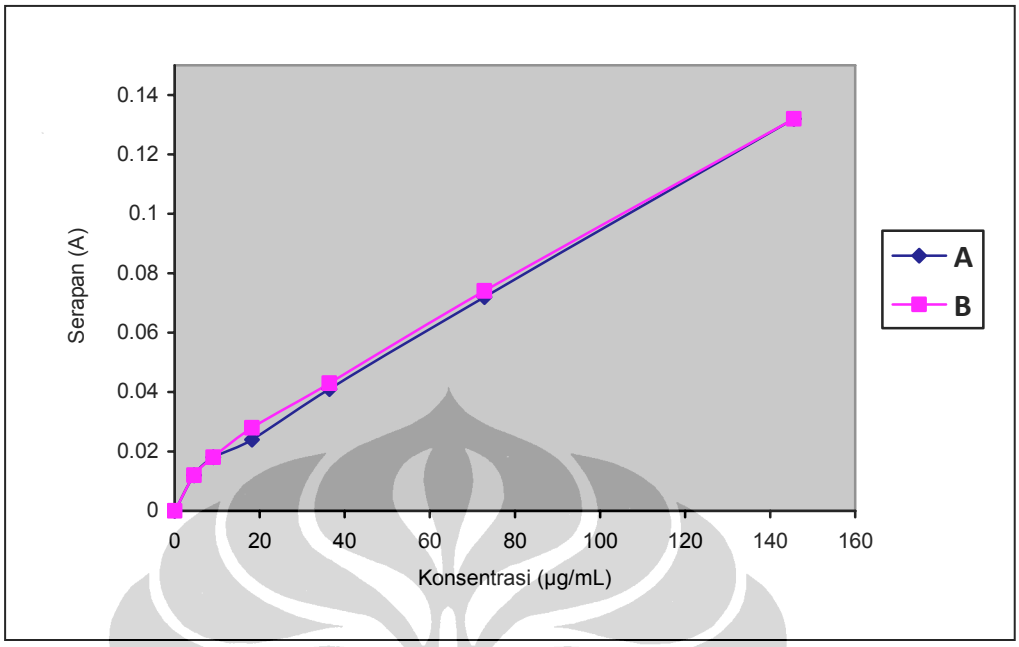
Keterangan :F4 = mikrokapsul alginat 4%-kitosan 0,3% berisi insulin 46,88 IU.
F5 = mikrokapsul alginat 4%-kitosan 0,3% berisi insulin 93,75 IU.
F6 = mikrokapsul alginat 4%-kitosan 0,3% berisi insulin 187,5 IU.



Gambar 17. Kurva kalibrasi BSA pada panjang gelombang 290 nm.

Keterangan : A = BSA dalam larutan asam klorida pH 1,2.
Persamaan garis : y = 0,0027 + 0,0001x.
Koefisien korelasi : r = 0,9971.

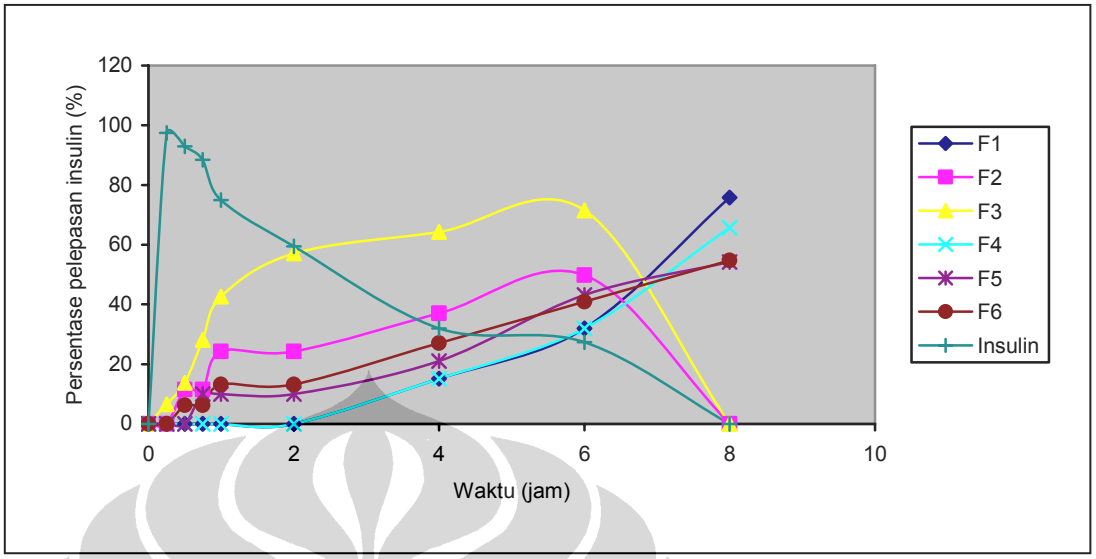
B = BSA dalam buffer fosfat pH 6,8.
Persamaan garis : y = 0,0028 + 0,0002x.
Koefisien korelasi : r = 0,9972.



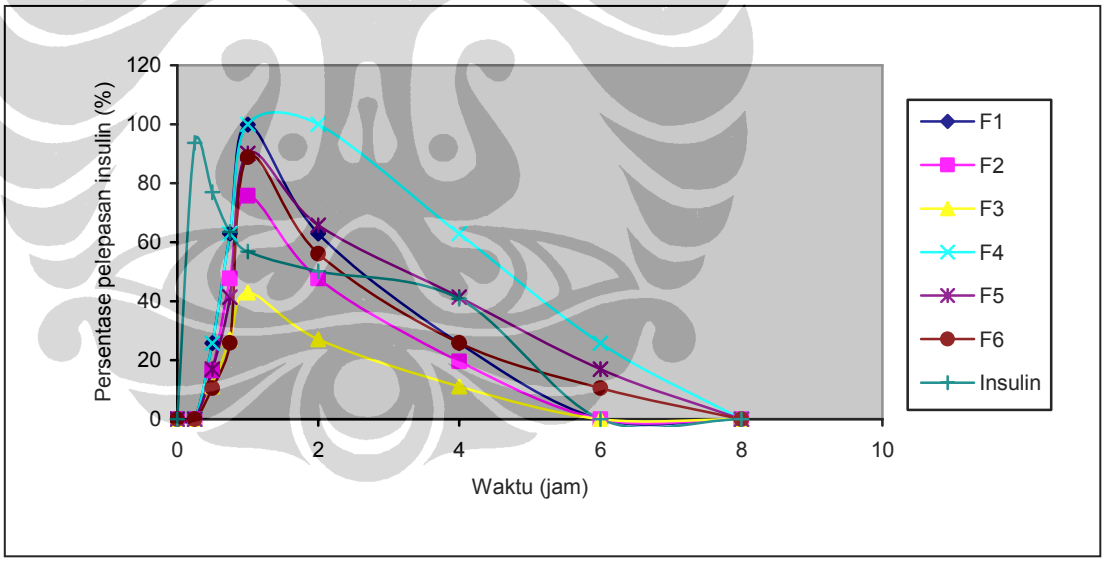
Gambar 18. Kurva kalibrasi insulin pada panjang gelombang 253 nm.

Keterangan : A = insulin dalam larutan asam klorida pH 1,2.
Persamaan garis : y = 0,0071 + 0,0009x
Koefisien korelasi : r = 0,9972.

B = insulin dalam buffer fosfat pH 6,8.
Persamaan garis : y = 0,0083 + 0,0009x
Koefisien korelasi : r = 0,9956



Gambar 19. Kurva profil pelepasan insulin dalam larutan asam klorida pH 1,2 pada panjang gelombang 253 nm.



Gambar 20. Kurva profil pelepasan insulin dalam buffer fosfat pH 6,8 pada panjang gelombang 253 nm.

TABEL

Tabel 2

Data distribusi ukuran partikel mikrokapsul alginat

Diameter (μm)	Mikrokapsul kosong alginat (%)				Mikrokapsul alginat berisi BSA (%)			
	2%	3%	4%	5%	2%	3%	4%	5%
0-23	0,000	1,236	5,035	0,112	0,387	0,374	0,000	0,000
24-45	40,900	48,758	51,809	40,613	42,211	40,699	36,504	34,864
46-89	54,234	41,056	31,790	52,265	49,070	49,161	54,489	55,927
90-175	4,866	7,657	8,600	6,441	8,205	8,925	8,469	8,641
176-263	0,000	1,383	2,315	0,270	0,810	1,141	0,539	0,566
Ukuran rata-rata	52,840 (μm)	54,062 (μm)	54,109 (μm)	54,274 (μm)	55,673 (μm)	56,604 (μm)	57,202 (μm)	57,819 (μm)

Tabel 3

Data distribusi ukuran partikel mikrokapsul alginat 3% tersalut kitosan

Diameter (μm)	Mikrokapsul kosong alginat-kitosan (%)			Mikrokapsul alginat-kitosan berisi BSA (%)		
	0,2%	0,3%	0,4%	0,2%	0,3%	0,4%
0-23	0,125	0,102	0,000	0,172	0,730	1,537
24-45	34,856	34,929	5,877	36,786	40,837	33,405
46-89	53,195	51,064	57,519	50,271	42,732	39,633
90-175	10,642	12,128	31,245	10,911	11,276	16,320
176-263	1,184	1,770	4,426	1,857	3,502	6,206
264-395	0,000	0,000	1,304	0,000	0,916	2,900
Ukuran rata-rata (μm)	60,036	61,949	67,850	60,758	64,440	68,453

Tabel 4

Data distribusi ukuran partikel mikrokapsul alginat 4% tersalut kitosan

Diameter (μm)	Mikrokapsul alginat kitosan kosong (%)			Mikrokapsul alginat kitosan berisi BSA (%)		
	0,2%	0,3%	0,4%	0,2%	0,3%	0,4%
0-23	0,136	2,673	0,422	0,000	3,263	0,167
24-45	30,470	37,097	11,852	19,264	18,843	5,75
46-89	48,469	26,845	25,408	46,895	24,21	14,999
90-175	16,925	14,167	26,337	24,74	32,758	25,451
176-263	3,546	11,238	15,627	6,825	15,144	20,933
264-395	0,495	0,000	9,651	2,275	5,006	15,454
396-778	0,000	0,000	3,918	0,000	0,543	10,808
Ukuran rata-rata	70,190 (μm)	98,977 (μm)	136,936 (μm)	88,281 (μm)	114,565 (μm)	198,347 (μm)

Tabel 5

Data distribusi ukuran partikel mikrokapsul 4% alginat berisi insulin

Diameter (μm)	Mikrokapsul alginat (%)		
	Insulin 46,88 IU	Insulin 93,75 IU	Insulin 187,5 IU
0-23	0,328	0,110	0,000
24-45	43,232	40,329	39,471
46-89	48,932	52,807	53,858
90-175	6,890	6,482	6,533
176-263	0,618	0,273	0,138
Ukuran rata-rata (μm)	54,281	54,383	54,492

Table 6

Data distribusi ukuran partikel mikrokapsul alginat 4%-0,3% kitosan berisi insulin

Diameter (μm)	Mikrokapsul alginat-kitosan (%)		
	Insulin 46,88 IU	Insulin 93,75 IU	Insulin 187,5 IU
0-23	2,404	2,668	2,121
24-45	23,888	17,880	24,812
46-89	30,270	22,878	25,507
90-175	25,123	26,542	18,765
176-263	11,294	15,946	14,839
264-395	4,372	7,060	10,063
396-679	0,447	1,358	3,897
Ukuran rata-rata (μm)	99,116	117,819	131,602

Tabel 7

Data perolehan berat mikrokapsul kosong alginat

No	Alginat (g)	Mikrokapsul alginat (g)
1	0,80	1,0763
2	0,80	1,0691
3	0,80	1,0592
4	1,20	1,6800
5	1,20	1,6711
6	1,20	1,6754
7	1,60	2,6001
8	1,60	2,5899
9	1,60	2,5925
10	2,00	2,6100
11	2,00	2,6121
12	2,00	2,6098

Tabel 8

Data perolehan berat mikrokapsul alginat berisi bovin serum albumin

No	Alginat (g)	Bovin serum albumin (mg)	Mikrokapsul alginat (g)
1	0,80	10,0	1,0753
2	0,80	10,0	1,0611
3	1,20	10,0	1,6821
4	1,20	10,0	1,6803
5	1,60	10,0	2,5981
6	1,60	10,0	2,6052
7	2,00	10,0	2,6110
8	2,00	10,0	2,6089

Tabel 9

Data perolehan berat mikrokapsul kosong alginat kitosan

No	Alginat (g)	Kitosan (g)	Mikrokapsul alginat kitosan (g)
1	1,20	0,4	1,6611
2	1,20	0,6	2,1235
3	1,20	0,8	2,3612
4	1,60	0,4	2,5810
5	1,60	0,6	2,6418
6	1,60	0,8	2,6450

Tabel 10

Data perolehan berat mikrokapsul alginat kitosan berisi bovin serum albumin

No	Alginat (g)	Kitosan (g)	Bovin serum albumin (mg)	Mikrokapsul (g)
1	1,20	0,4	10,0	1,6754
2	1,20	0,6	10,0	2,1391
3	1,20	0,8	10,0	2,3581
4	1,60	0,4	10,0	2,5823
5	1,60	0,6	10,0	2,6420
6	1,60	0,8	10,0	2,6457

Tabel 11

Data perolehan berat mikrokapsul alginat berisi insulin

No	Alginat (g)	Insulin (mg)	Mikrokapsul insulin (g)
1	1,60	1,7064	2,3535
2	1,60	3,4125	2,3621
3	1,60	6,8250	2,3672

Tabel 12

Data perolehan berat mikrokapsul alginat kitosan berisi insulin

No	Alginat (g)	Kitosan (g)	Insulin (mg)	Mikrokapsul (g)
1	1,60	0,6	1,7064	2,4134
2	1,60	0,6	3,4125	2,6212
3	1,60	0,6	6,8250	2,6335

Tabel 13

Data penetapan kadar air mikrokapsul kosong alginat

No	Alginat (%)	Mikrokapsul alginat kosong (mg)	Kadar air (%)
1	2,0	200	8,29
2	2,0	200	8,32
3	2,0	200	8,35
4	3,0	200	8,42
5	3,0	200	8,45
6	3,0	200	8,49
7	4,0	200	8,65
8	4,0	200	8,61
9	4,0	200	8,68
10	5,0	200	871
11	5,0	200	8,77
12	5,0	200	8,79

Tabel 14

Data penetapan kadar air mikrokapsul alginat berisi bovin serum albumin

No	Alginat (%)	Mikrokapsul alginat kosong (mg)	Kadar air (%)
1	2,0	200	8,28
2	2,0	200	8,34
3	3,0	200	8,44
4	3,0	200	8,46
5	4,0	200	8,67
6	4,0	200	8,69
7	5,0	200	873
8	5,0	200	8,70

Tabel 15

Data penetapan kadar air mikrokapsul kosong alginat kitosan

No	Alginat (%)	Kitosan (%)	Mikrokapsul (mg)	Kadar air (%)
1	3,0	0,2	100	8,69
2	3,0	0,3	100	8,72
3	3,0	0,4	100	8,81
4	4,0	0,2	100	8,71
5	4,0	0,3	100	8,78
6	4,0	0,4	100	8,84

Tabel 16

Data penetapan kadar air mikrokapsul alginat kitosan berisi bovin serum albumin

No	Alginat (%)	Kitosan (%)	BSA (mg)	Mikrokapsul (g)	Kadar air (%)
1	3,0	0,2	10,0	100	8,71
2	3,0	0,3	10,0	100	8,74
3	3,0	0,4	10,0	100	8,83
4	4,0	0,2	10,0	100	8,73
5	4,0	0,3	10,0	100	8,80
6	4,0	0,4	10,0	100	8,83

Tabel 17

Data penetapan kadar air mikrokapsul alginat berisi insulin

No	Alginat (%)	Insulin (mg)	Mikrokapsul (mg)	Kadar air (%)
1	4,0	1,7064	200	8,12
2	4,0	3,4125	200	8,14
3	4,0	6,8250	200	8,19

Tabel 18

Data penetapan kadar air mikrokapsul alginat kitosan berisi insulin

No	Alginat (%)	Kitosan (%)	Insulin (mg)	Mikrokapsul (mg)	Kadar air (%)
1	4,0	0,3	1,7064	200	8,69
2	4,0	0,3	3,4125	200	8,73
3	4,0	0,3	6,8250	200	8,79

Tabel 19

Data kurva kalibrasi bovin serum albumin dalam larutan asam klorida pH 1,2

Konsentrasi (µg/mL)	Serapan (A)
0	0
1,5625	0,001
3,125	0,003
12,5	0,005
25	0,005
50	0,007
6,25	0,010
100	0,018
200	0,032
400	0,059

Keterangan :
Persamaan garis : y = 0,0027 + 0,0001x
Koefisien korelasi : r = 0,9971

Kondisi percobaan :
Volume pengukuran 150 µl
Larutan asam klorida pH 1,2
Detektor Uv-Vis, panjang gelombang 290 nm

Tabel 20

Data kurva kalibrasi bovin serum albumin dalam buffer fosfat pH 6,8

Konsentrasi (µg/mL)	Serapan (A)
0	0
1,5625	0,001
3,125	0,003
6,25	0,005
12,5	0,006
25	0,007
50	0,011
100	0,019
200	0,034
400	0,062

Keterangan :
Persamaan garis : y = 0,0028 + 0,0002x
Koefisien korelasi : r = 0,9972

Kondisi percobaan :
Volume pengukuran 150 µl
Larutan buffer fosfat pH 6,8
Detektor Uv-Vis, panjang gelombang 290 nm

Tabel 21

Data kurva kalibrasi insulin dalam larutan asam klorida pH 1,2

Konsentrasi (µg/mL)	Serapan (A)
0	0
4,55	0,012
9,1	0,018
18,2	0,024
36,4	0,041
72,8	0,072
145,6	0,132

Keterangan :
Persamaan garis : y = 0,0071 + 0,0009x
Koefisien korelasi : r = 0,9972

Kondisi percobaan :
Volume pengukuran 150 µl
Larutan asam klorida pH 1,2
Detektor Uv-Vis, panjang gelombang 253 nm

Tabel 22

Data kurva kalibrasi insulin dalam buffer fosfat pH 6,8

Konsentrasi (µg/mL)	Serapan (A)
0	0
4,55	0,012
9,1	0,018
18,2	0,028
36,4	0,043
72,8	0,074
145,6	0,132

Keterangan :
Persamaan garis : y = 0,0083 + 0,0009x
Koefisien korelasi : r = 0,9956

Kondisi percobaan :
Volume pengukuran 150 µl
Larutan buffer fosfat pH 6,8
Detektor Uv-Vis, panjang gelombang 253 nm

Tabel 23

Data persentase BSA dalam mikrokapsul alginat

Alginat (%)	Bobot total (g)	Bobot analisa (g)	Kadar dlm larutan asam klorida (mg)	Kadar dlm buffer fosfat (mg)	Kadar total (mg)	Berat BSA awal (mg)	Efisiensi (%)
2,0	0,9856	0,0917	5,7	1,4	7,1	10,0	71
2,0	0,9732	0,0917	5,6	1,4	7,0	10,0	70
3,0	1,5397	0,0916	2,2	5,9	8,1	10,0	81
3,0	1,5385	0,0915	2,2	5,9	8,1	10,0	81
4,0	2,3728	0,0913	0	9,1	9,1	10,0	91
4,0	2,3788	0,0913	0	9,1	9,1	10,0	91
5,0	2,3830	0,0913	0	9,1	9,1	10,0	91
5,0	2,3819	0,0913	0	9,1	9,1	10,0	91

Tabel 24

Data persentase BSA dalam mikrokapsul alginat-kitosan

Alginat (%)	Kitosan (%)	Berat BSA awal (mg)	Bobot total (g)	Bobot analisa (g)	Kadar dlm larutan asam klorida (mg)	Kadar dlm buffer fosfat (mg)	Kadar total (mg)	Efisiensi (%)
3,0	0,2	10,0	1,5293	0,0913	2,2	5,9	8,1	81
3,0	0,3	10,0	1,9521	0,0913	0,6	7,5	8,1	81
3,0	0,4	10,0	2,1499	0,0912	0	8,3	8,3	83
4,0	0,2	10,0	2,3569	0,0913	0	9,1	9,1	91
4,0	0,3	10,0	2,4095	0,0912	0	9,3	9,3	93
4,0	0,4	10,0	2,4121	0,0912	0	9,3	9,3	93

Tabel 25

Data persentase insulin dalam mikrokapsul alginat

Alginat (%)	Berat insulin awal (mg)	Bobot total (g)	Bobot analisa (g)	Kadar dlm larutan asam klorida (mg)	Kadar dlm buffer fosfat (mg)	Kadar total (mg)	Efisiensi (%)
4,0	1,7064	2,1624	0,0919	0	1,553	1,553	91,0
4,0	3,4125	2,1698	0,0919	0,496	1,558	2,054	60,2
4,0	6,8250	2,1733	0,0918	2,078	1,563	3,641	53,3

Tabel 26

Data persentase insulin dalam mikrokapsul alginat-kitosan

Alginat (%)	Kitosan (%)	Berat insulin awal (mg)	Bobot total (g)	Bobot analisa (g)	Kadar dlm larutan asam klorida (mg)	Kadar dlm buffer fosfat (mg)	Kadar total (mg)	Efisiensi (%)
4,0	0,3	1,7064	2,2037	0,0913	0	1,593	1,593	93,4
4,0	0,3	3,4125	2,3924	0,0913	0,262	2,369	2,631	77,1
4,0	0,3	6,8250	2,4020	0.0912	0,556	3,669	4,225	61,9

Tabel 27

Profil pelepasan mikrokapsul insulin dalam larutan asam klorida pH 1,2

Jam ke -	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	Insulin (%)
0	0	0	0	0	0	0	0
0,25	0	0	6,50	0	0	0	97,5
0,50	0	11,50	16,96	0	0	6,23	80,69
0,75	0	17,25	36,65	0	9,96	9,35	72,29
1	0	32,85	42,50	0	14,94	17,82	68,08
2	0	40,64	65,88	0	17,43	22,06	61,40
4	15,15	57,32	75,57	15,15	29,75	38,04	30,70
6	39,57	78,42	80,41	39,57	58,02	59,89	15,35
8	95,58	39,21	63,38	85,43	83,23	84,67	7,68

Keterangan : F1 = Mikrokapsul alginat berisi insulin 46,88 IU.
F2 = Mikrokapsul alginat berisi insulin 93,75 IU.
F3 = Mikrokapsul alginat berisi insulin 187,50 IU.
F4 = Mikrokapsul alginat-kitosan berisi insulin 46,88 IU.
F5 = Mikrokapsul alginat-kitosan berisi insulin 93,75 IU .
F6 = Mikrokapsul alginat-kitosan berisi insulin 187,50 IU.

Tabel 28

Profil pelepasan mikrokapsul insulin dalam buffer fosfat pH 6,8

Jam ke -	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	Insulin (%)
0	0	0	0	0	0	0	0
0,25	0	0	0	0	0	0	93,74
0,50	25,76	19,52	11.05	25,76	16,93	10,59	87,73
0,75	75,85	57,49	32,55	75,85	49,86	31,21	84,73
1	100	76,48	59,18	100	90,66	71,70	83,22
2	75,76	57,76	56,61	100	86,72	61,76	41,61
4	37,88	28,88	39,36	75,76	60,29	30,88	21,80
6	18,94	14,44	19,68	37,88	30,14	15,44	10,40
8	9,47	7,22	9,84	18,94	15,07	7,72	5,20

Keterangan: F1 = Mikrokapsul alginat berisi insulin 46,88 IU.
F2 = Mikrokapsul alginat berisi insulin 93,75 IU.
F3 = Mikrokapsul alginat berisi insulin 187,50 IU.
F4 = Mikrokapsul alginat-kitosan berisi insulin 46,88 IU.
F5 = Mikrokapsul alginat-kitosan berisi insulin 93,75 IU.
F6 = Mikrokapsul alginat-kitosan berisi insulin 187,50 IU.

LAMPIRAN

Lampiran 1

Cara perhitungan nilai persentase zat inti dalam mikrokapsul

A. Cara perhitungan nilai persentase BSA dalam mikrokapsul

Persamaan kurva kalibrasi BSA dalam larutan asam klorida pH 1,2

$y = 0,0027 + 0,0001x$

y = serapan (A)

x = konsentrasi (µg/mL)

Persamaan kurva kalibrasi BSA dalam larutan buffer fosfat pH 6,8

$y = 0,0028 + 0,0002x$

y = serapan (A)

x = konsentrasi (µg/mL)

contoh :

Serapan BSA dalam larutan asam klorida pH 1,2 adalah 0,008 dan serapan BSA dalam buffer fosfat pH 6,8 adalah 0,004. Volume larutan asam klorida 10,0 mL. Volume buffer fosfat + NaOH + alkohol adalah 22,0 mL. Berat mikrokapsul analisa 0,0917 g. Berat total mikrokapsul 0,9856 g. Berat BSA awal formulasi 10,0 mg.

Kadar dalam larutan asam klorida pH 1,2:

0,008 = 0,0027 + 0,0001x

x = 53 µg/mL

untuk 10 mL = 530 µg = 0,053 mg

untuk 0,0917 g mikrokapsul = 0,053 mg BSA

untuk 0,9856 g mikrokapsul = $\frac{0,9856\ g}{0,0917\ g}$ x 0,053 = 5,7 mg

Kadar dalam buffer fosfat pH 6,8:

0,004 = 0,0028 + 0,0002x

x = 6 µg/mL

untuk 22 mL = 132 µg = 0,132 mg

untuk 0,0917 g mikrokapsul = 0,132 mg BSA

untuk 0,9856 g mikrokapsul = $\frac{0,9856\ g}{0,0917\ g}$ x 0,132 = 1,4 mg

Persentase BSA dalam mikrokapsul = $\frac{5,7\ mg + 1,4\ mg}{10,0\ mg}$ x 100%= 71%

B. Cara perhitungan nilai persentase insulin dalam mikrokapsul

Persamaan kurva kalibrasi insulin dalam larutan asam klorida pH 1,2

y = 0,0071 + 0,0009x

y = serapan (A)

x = konsentrasi (µg/mL)

Persamaan kurva kalibrasi insulin dalam larutan buffer fosfat pH 6,8

$y = 0,0083 + 0,0009x$

y = serapan (A)

x = konsentrasi (µg/mL)

contoh :

Serapan insulin dalam larutan asam klorida pH 1,2 adalah 0,009 dan serapan insulin dalam buffer fosfat pH 6,8 adalah 0,011. Volume larutan asam klorida 10,0 mL. Volume buffer fosfat + NaOH + alkohol adalah 22,0 mL. Berat mikrokapsul analisa 0,0919 g. Berat total mikrokapsul 2,1698 g. Berat insulin awal formulasi 3,4125 mg.

Kadar dalam larutan asam klorida pH 1,2:

$0,009 = 0,0083 + 0,0009x$

x = 0,78 µg/mL

untuk 10 mL = 7,8 µg = 0,0078 mg

untuk 0,0919 g mikrokapsul = 0,0078 mg insulin

untuk 2,1698 g mikrokapsul = $\frac{2,1698\ g}{0,0919\ g} \times 0,021 = 0,496$ mg

Kadar dalam buffer fosfat pH 6,8:

$0,011 = 0,0083 + 0,0009x$

x = 3 µg/mL

untuk 22 mL = 66 µg = 0,066 mg

untuk 0,0919 g mikrokapsul = 0,066 mg insulin

untuk 2,1698 g mikrokapsul = $\frac{2.1698\ g}{0,0919\ g}$ x 0,066 = 1,558 mg

Persentase insulin dalam mikrokapsul=$\frac{0,496\ mg + 1,558\ mg}{3,4125\ mg}$ x 100%= 60,2%

Lampiran 2

Rumus perhitungan nilai pelepasan insulin dalam mikrokapsul

A. Rumus perhitungan nilai pelepasan insulin dalam mikrokapsul pada larutan asam klorida pH 1,2

y = 0,0071 + 0,0009x

y = serapan (A)

x = konsentrasi (µg/mL)

$$C1 = C_{\text{kurva kalibrasi}} \times \frac{\text{V larutan}}{\text{Bobot insulin}} \times 100\%$$

$$C2 = C_{\text{kurva kalibrasi}} \times \frac{\text{V larutan}}{\text{Bobot insulin}} \times 100\% + (\text{Vsampel} \times C1)$$

$$C3 = C_{\text{kurva kalibrasi}} \times \frac{\text{V larutan}}{\text{Bobot insulin}} \times 100\% + (\text{Vsampel} \times C1) + (\text{Vsampel} \times C2)$$

B. Rumus perhitungan nilai pelepasan insulin dalam mikrokapsul pada larutan buffer fosfat pH 6,8

Persamaan kurva kalibrasi insulin dalam larutan buffer fosfat pH 6,8

y = 0,0083 + 0,0009x

y = serapan (A)

x = konsentrasi (µg/mL)

$$C1 = C_{\text{kurva kalibrasi}} \times \frac{\text{V larutan}}{\text{Bobot insulin}} \times 100\%$$

$$C2 = C_{\text{kurva kalibrasi}} \times \frac{\text{V larutan}}{\text{Bobot insulin}} \times 100\% + (\text{Vsampel} \times C1)$$

$$C3 = C_{\text{kurva kalibrasi}} \times \frac{\text{V larutan}}{\text{Bobot insulin}} \times 100\% + (\text{Vsampel} \times C1) + (\text{Vsampel} \times C2)$$

Lampiran 3

Sertifikat analisis alginat

SIGMA-ALDRICH

Certificate of Analysis

Product Name	Alginic acid sodium salt from brown algae, Low viscosity
Product Number	A2158
Product Brand	Sigma
CAS Number	9005-38-3

TEST	SPECIFICATION	LOT 114K0177 RESULTS
APPEARANCE	OFF-WHITE TO LIGHT TAN POWDER	LIGHT TAN POWDER
SOLUBILITY	HAZY FAINT YELLOW SOLUTION AT 100 MG PLUS 10 ML OF WATER	CONFORMS
BROOKFIELD VISCOSITY	APPROX. 250 CPS (2% IN WATER AT 25 DEG CENTRIGRADE)	237 CPS (SUPPLIER TEST RESULT)
QC RELEASE DATE		NOVEMBER 2004

Rodney Burbach, Supervisor
Analytical Services
St. Louis, Missouri USA

Lampiran 4

Sertifikat analisis kitosan

SIGMA-ALDRICH

Certificate of Analysis

Product Name	Chitosan from crab shells, ≥75% (deacetylated)
Product Number	C3646
Product Brand	Sigma
CAS Number	9012-76-4

TEST	SPECIFICATION	LOT 086K0067 RESULTS
APPEARANCE	WHITE TO TAN POWDER AND FLAKES	OFF-WHITE
SOLUBILITY	HAZY FAINT YELLOW SOLUTION AT 50 MG PLUS 5 ML OF 1 M ACETIC ACID	CONFORMS
DEACETYLATION	MINIMUM 75%	75%
QC RELEASE DATE		AUGUST 2006

Rodney Burbach, Supervisor
Analytical Services
St. Louis, Missouri USA

Lampiran 5

Sertifikat analisis bovin serum albumin

SIGMA-ALDRICH

Certificate of Analysis

Product Name	Albumin from bovine serum, for molecular biology, powder
Product Number	B4287
Product Brand	Sigma
CAS Number	9048-46-8
Storage Temp	2-8°C

TEST	SPECIFICATION	LOT 036K07341 RESULTS
APPEARANCE	WHITE TO YELLOW WITH A LIGHT TAN OR GREEN CAST POWDER	OFF-WHITE POWDER
SOLUBILITY	CLEAR TO SLIGHTLY HAZY LIGHT YELLOW TO YELLOW-GREEN SOLUTION AT 40MG/ML IN WATER	CLEAR FAINT YELLOW
PROTEASE	NONE DETECTED	PASS
SUITABILITY TEST	SUITABLE FOR BLOCKING NON-SPECIFIC PROTEIN BINDING SITES IN HYBRIDIZATIONS	SUITABLE
AGAROSE ELECTROPHORESIS		>99%
VSV VIRUS (IFA METHOD)		NOT DETECTED
BT VIRUS (IFA METHOD)		NOT DETECTED
INACTIVATION PROCESS		PH NOT MORE THAN 5.0 FOR AT LEAST 2 HOURS; TEMPERATURE NOT LESS THAN 65 DEG C FOR NOT LESS THAN 3 HOURS
QC RELEASE DATE		NOVEMBER 2006

Rodney Burbach, Supervisor
Analytical Services
St. Louis, Missouri USA

Lampiran 6

Keterangan produk insulin

This package insert is continually updated:
please read carefully before using a new pack!

LANTUS®
100 IU/ml solution for injection in a vial

Active ingredient: Insulin glargine

Aventis

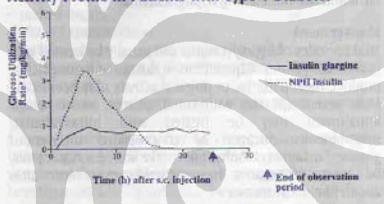
Insulin with a long and steady blood-sugar-lowering action

Composition
Each ml of the solution for injection contains 3.64 mg of the active substance insulin glargine, corresponding to 100 IU human insulin. Each pen contains 3 ml, equivalent to 300 IU.
Excipients: Polysorbate 80, zinc chloride, m-cresol, glycerol, hydrochloric acid, sodium hydroxide, water for injections.
Insulin glargine is an insulin analogue produced by recombinant DNA technology using *Escherichia coli* (K 12 strains).

Pharmacological properties
Pharmacodynamic properties
Pharmacotherapeutic group: Antidiabetic agent. Insulin and analogues, long-acting. ATC Code: A10A E04.
Insulin glargine is a human insulin analogue designed to have a low solubility at neutral pH. It is completely soluble at the acidic pH of the Lantus injection solution (pH 4). After injection into the subcutaneous tissue, the acidic solution is neutralised leading to formation of micro-precipitates from which small amounts of insulin glargine are continuously released, providing a smooth, peakless, predictable concentration/time profile with a prolonged duration of action.

Insulin receptor binding: Insulin glargine is very similar to human insulin with respect to insulin receptor binding kinetics. It can, therefore, be considered to mediate the same type of effect via the insulin receptor as insulin.
The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogues lower blood glucose levels by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis.
In clinical pharmacology studies, intravenous insulin glargine and human insulin have been shown to be equipotent when given at the same doses. As with all insulins, the time course of action of insulin glargine may be affected by physical activity and other variables.
In euglycaemic clamp studies in healthy subjects or in patients with type 1 diabetes, the onset of action of subcutaneous insulin glargine was slower than with human NPH insulin, its effect profile was smooth and peakless, and the duration of its effect was prolonged.
After subcutaneous injection of 0.3 IU/kg insulin glargine in diabetic patients, a flat concentration-time profile has been demonstrated..
The following graph shows the results from a study in patients:

Activity Profile in Patients with Type 1 Diabetes



* determined as amount of glucose infused to maintain constant plasma glucose levels (hourly mean values).

The longer duration of action of insulin glargine is directly related to its slower rate of absorption and supports once daily administration. The time course of action of insulin and insulin analogues such as insulin glargine may vary considerably in different individuals or within the same individual.

In a clinical study, symptoms of hypoglycaemia or counter-regulatory hormone responses were similar after intravenous insulin glargine and human insulin both in healthy volunteers and patients with type 1 diabetes.

Pharmacokinetic properties
In healthy subjects and diabetic patients, insulin serum concentrations indicated a slower and much more prolonged absorption and showed a lack of a peak after subcutaneous injection of insulin glargine in comparison to human NPH insulin. Concentrations were thus consistent with the time profile of the pharmacodynamic activity of insulin glargine. The graph above shows the activity profiles over time of insulin glargine and NPH insulin.
The median time between injection of the drug and the end of its pharmacological effect was 14.5 hours for NPH insulin while the median time for insulin glargine was 24 hours (the end of the observation period).
In studies in type 1 and type 2 diabetes mellitus patients, the overall efficacy of once-daily insulin glargine on metabolic control was compared to that of once-daily and twice-daily NPH human insulin. In general, insulin glargine maintained or improved the level of glycaemic control as measured by glycohaemoglobin and fasting glucose.
In addition, fewer patients using insulin glargine reported a hypoglycaemic episodes compared to patients using NPH human insulin.
Insulin glargine injected once daily will reach steady state levels in 2-4 days after the first dose.
When given intravenously the elimination half-life of insulin glargine and human insulin were comparable.
In man, insulin glargine is partly degraded in the subcutaneous tissue at the carboxyl terminus of the Beta chain with formation of the active metabolites 21A-Gly-insulin and 21A-Gly-des-30B-Thr-insulin. Unchanged insulin glargine and degradation products are also present in the plasma.
In clinical studies, subgroup analyses based on age and gender did not indicate any difference in safety and efficacy in insulin glargine-treated patients compared to the entire study population.

Preclinical safety data
Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

Therapeutic indications
For the treatment of adults, adolescents and children of 6 years or above with diabetes mellitus, where treatment with insulin is required.

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Contraindications

Hypersensitivity to insulin glargine or to any of the excipients.

Posology and method of administration

Lantus contains insulin glargine an insulin analogue with a prolonged duration of action. It should be administered once daily at any time but at the same time each day.

The dosage and timing of dose of Lantus should be individually adjusted. In patients with type 2 diabetes mellitus, Lantus can also be given together with orally active antidiabetic medicinal products.

Children

In children efficacy and safety of Lantus have only been demonstrated when given in the evening.

Due to limited experience the efficacy and safety of Lantus have not been demonstrated in children below the age of 6 years.

Transition from other insulins to Lantus

When changing from a treatment regimen with an intermediate or long-acting insulin to a regimen with Lantus, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic agents).

To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with Lantus should reduce their daily dose of basal insulin by 20-30% during the first weeks of treatment

During the first weeks the reduction should, at least partially, be compensated by an increase in mealtime insulin, after this period the regimen should be adjusted individually.

As with other insulin analogues, patients with high insulin doses because of antibodies to human insulin may experience an improved insulin response with Lantus.

Close metabolic monitoring is recommended during the transition and in the initial weeks thereafter.

With improved metabolic control and resulting increase in insulin sensitivity a further adjustment in dosage regimen may become necessary. Dose adjustment may also be required, for example, if the patient's weight or life-style changes, change of timing of insulin dose or other circumstances arise that increase susceptibility to hypo-or hyperglycaemia.

Administration

Lantus is administered subcutaneously.

Lantus should not be administered intravenously. The prolonged duration of action of Lantus is dependent on its injection into subcutaneous tissue. Intravenous administration of the usual subcutaneous dose could result in severe hypoglycaemia.

There are no clinically relevant differences in serum insulin or glucose levels after abdominal, deltoid or thigh administration of Lantus. Injection sites must be rotated within a given injection area from one injection to the next.

Lantus must not be mixed with any other insulin or diluted. Mixing or diluting can change its time/action profile and mixing can cause precipitation.

Due to limited experience the efficacy and safety of Lantus could not be assessed in the following groups of patients: patients with impaired liver function or patients with moderate/severe renal impairment .

Syringes must not contain any other medicines or traces thereof.

Once opened, the vial may be used for up to four weeks when stored below 25 °C and protected from heat and light.

Overdose

Symptoms

Insulin overdose may lead to severe and sometimes long-term and life-threatening hypoglycaemia.

Management

Mild episodes of hypoglycaemia can usually be treated with oral carbohydrates. Adjustments in dosage of the medicinal product, meal patterns, or physical activity may be needed.

More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

Special warnings and special precautions for use

Lantus is not the insulin of choice for the treatment of diabetic ketoacidosis. Instead, regular insulin administered intravenously is recommended in such cases.

Safety and efficacy of Lantus has been established in adolescents and children of 6 years and above.

Due to limited experience the efficacy and safety of Lantus could not be assessed in children below 6 years of age, in patients with impaired liver function or in patients with moderate/severe renal impairment.

In patients with renal impairment, insulin requirements may be diminished due to reduced insulin metabolism. In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements.

In patients with severe hepatic impairment, insulin requirements may be diminished due to reduced capacity for gluconeogenesis and reduced insulin metabolism.

In case of insufficient glucose control or a tendency to hyper- or hypoglycaemic episodes, the patient's adherence to the prescribed treatment regimen, injection sites and proper injection technique and all other relevant factors must be reviewed before dose adjustment is considered.

Patients must be instructed in the skills necessary for the self-management of diabetes, such as blood sugar monitoring, proper injection technique, measures for recognising and managing reduced or increased blood sugar levels (**hypo -** or **Hyperglycaemia**) as described below. In addition, they must learn how to handle special situations such as skipped, inadequate or increased insulin doses, inadequate food intake or missed meals. Moreover, patients and their relatives must learn how to recognise the signs and symptoms of hypo- or hyperglycaemia, what corrective actions need to be taken and when they must speak with their doctor.

Hypoglycaemia

The time of occurrence of hypoglycaemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen is changed. Due to more sustained basal insulin supply with Lantus, less nocturnal but more early morning hypoglycaemia can be expected.

Hypoglycaemia is more likely to occur at the start of insulin treatment, following transfer to a different insulin preparation, where metabolic control is unstable, or in severe kidney or liver diseases.

Symptoms that may indicate the onset of hypoglycaemia may be, e.g., sweating, clammy skin, anxiety, fast heart beat, high blood pressure, palpitations and irregular heart beat, chest pain (angina pectoris). In many patients, these signs and symptoms often develop before those of a low sugar level in the brain. The latter include headache, intense hunger,

nausea, vomiting, tiredness, sleepiness, sleep disturbances, restlessness, aggressive behaviour, lapses in concentration, impaired reactions, depression, confusion, speech disturbances (sometimes total loss of speech), visual disorders, trembling, paralysis, tingling sensations (paraesthesiae) numbness and tingling sensations in the area of the mouth, dizziness, loss of self-control, inability to look after oneself, convulsions, and loss of consciousness.

The initial symptoms pointing to the onset of hypoglycaemia ("warning symptoms") may change be milder, or be entirely absent, e.g., in the following circumstances: markedly improved blood sugar control, slow-developing hypoglycaemia, advanced age, a certain type of nervous disease (autonomic neuropathy), long-standing diabetes, a psychiatric illness, or concurrent use of other medicines (see " Interactions"). In such circumstances, severe hypoglycaemia (and even loss of consciousness) may develop without the patients noticing it. Affected patients should try to keep familiar at all times with their individual warning symptoms. More frequent blood sugar testing can help to identify mild hypoglycaemic episodes which otherwise might be overlooked. Patients not confident of recognising their warning symptoms should avoid situations (e.g. driving a car) that might result in danger to themselves or others.

Particular caution should be exercised, and intensified blood glucose monitoring is advisable in patients in whom hypoglycaemic episodes might be of particular clinical relevance, such as in patients with significant stenoses of the coronary arteries or of the blood vessels supplying the brain (risk of cardiac or cerebral complications of hypoglycaemia) as well as in patients with proliferative retinopathy, particularly if not treated with photocoagulation (risk of transient amaurosis following hypoglycaemia).

Patients should be aware of circumstances where warning symptoms of hypoglycaemia are diminished. The warning symptoms of hypoglycaemia may be changed, be less pronounced or be absent in certain risk groups. These include patients:

- in whom glycaemic control is markedly improved,
- in whom hypoglycaemia develops gradually,
- who are elderly,
- after transfer from animal insulin to human insulin,
- in whom an autonomic neuropathy is present,
- with a long history of diabetes,
- suffering from a psychiatric illness,
- receiving concurrent treatment with certain other medicinal products (see section 4.5).

Such situations may result in severe hypoglycaemia (and possibly loss of consciousness) prior to the patient's awareness of hypoglycaemia.

The prolonged effect of subcutaneous insulin glargine may delay recovery from hypoglycaemia.

If normal or decreased values for glycated haemoglobin are noted, the possibility of recurrent, unrecognised (especially nocturnal) episodes of hypoglycaemia must be considered.

Adherence of the patient to the dosage and dietary regimen, correct insulin administration and awareness of hypoglycaemia symptoms are essential to reduce the risk of hypoglycaemia. Factors increasing the susceptibility to hypoglycaemia require particularly close monitoring and may necessitate dose adjustment. These include:

- change in the injection area,
- improved insulin sensitivity (by, e.g., removal of stress factors),
- unaccustomed, increased or prolonged physical activity,
- intercurrent illness (e.g. vomiting, diarrhoea),
- inadequate food intake,
- missed meals,
- alcohol consumption,
- certain uncompensated endocrine disorders, (e.g. in hypothyroidism and in anterior pituitary or adrenocortical insufficiency),
- concomitant treatment with certain other medicinal products.

A hypoglycaemic attack can be corrected by immediately taking sugar, e.g., in the form of glucose, sugar cubes or sugar-sweetened beverages. In this regard, please note that food or beverages containing artificial sweeteners (e.g. diet foods and drinks) are not suitable. Subsequently, some food having a long -acting blood -sugar-raising effect (e.g. bread) should be taken. The long action of Lantus may delay recovery from hypoglycaemia. If hypoglycaemia recurs, another 10 to 20 g of sugar should be taken. If a hypoglycaemia attack cannot be corrected or if it recurs, speak to a doctor immediately.

Carry at least 20 grams of sugar with you at all times, together with some information identifying you as a diabetic. Inability to swallow or unconsciousness will make necessary injections of glucose solution or glucagon (a medicine increasing blood sugar), even where the presence of hypoglycaemia is uncertain.

Following intake of glucose, hypoglycaemia should be conformed by means of blood sugar testing.

Please inform your doctor in the event of intercurrent illness, since this situation necessitates intensified metabolic monitoring and , possibly, further special measures (e.g., dose adjustment, urine tests for ketones).

Hyperglycaemia may occur under certain circumstances. These include:

- omission or reduction of injections or decrease in insulin effectiveness (e.g. due to incorrect storage)
- pen malfunction
- decreased physical activity, stress situations (emotional distress, excitement), injuries, operations, feverish illnesses or certain other diseases
- concurrent use of other medicines (see " Interactions")

Thirst, increased need to pass water , tiredness, dry skin, reddening of the face, loss of appetite, low blood pressure, fast heart beat and high concentrations of sugar and ketone bodies in the urine may be signs of hyperglycaemia. Stomach pain, fast and deep breathing, sleepiness or even loss of consciousness may be signs of a serious metabolic condition (ketoacidosis) resulting from lack of insulin. Blood sugar testing or tests for ketones in urine must be carried out as soon as any such symptoms occur. Severe hyperglycaemia or ketoacidosis must always be treated by a doctor, normally in a hospital.

Intercurrent illness

Intercurrent illness requires intensified metabolic monitoring. In many cases urine tests for ketones are indicated, and often it is necessary to adjust the insulin dose. The insulin requirement is often increased. Patients with type 1 diabetes must continue to consume at least a small amount of carbohydrates on a regular basis, even if they are able to eat only little or no food, or are vomiting etc. and they must never omit insulin entirely.

Pregnancy and lactation

For insulin glargin no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal /foetal development, parturition or postnatal development .

Caution should be exercised when prescribing to pregnant women.

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It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential.
Lactating women may require adjustments in insulin dose and diet.

Effects on ability to drive and use machines
The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia or hyperglycaemia or, for example, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).
Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia. It should be considered whether it is advisable to drive or operate machinery in these circumstances.

Interaction
A number of substances affect glucose metabolism and may require dose adjustment of insulin glargine.
Substances that may enhance the blood-glucose-lowering effect and increase susceptibility to hypoglycaemia include oral antidiabetic agents, ACE inhibitors, disopyramide, fibrates, fluoxetine, MAO inhibitors, pentoxifylline, propoxyphene, salicylates and sulfonamide antibiotics.
Substances that may reduce the blood-glucose-lowering effect include corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, oestrogens and progestogens, phenothiazine derivatives, somatropin, sympathomimetic agents (e.g. epinephrine [adrenaline], salbutamol, terbutaline) and thyroid hormones.
Beta-blockers, clonidine, lithium salts or alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycaemia, which may sometimes be followed by hyperglycaemia.
In addition, under the influence of sympatholytic medicinal products such as beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation may be reduced or absent.

Undesirable effects
Hypoglycaemia
Hypoglycaemia, in general the most frequent undesirable effect of insulin therapy, may occur if the insulin dose is too high in relation to the insulin requirement. Severe hypoglycaemic attacks, especially if recurrent, may lead to neurological damage. Prolonged or severe hypoglycaemic episodes may be life-threatening.
In many patients, the signs and symptoms of neuroglycopenia are preceded by signs of adrenergic counter-regulation. Generally, the greater and more rapid the decline in blood glucose, the more marked is the phenomenon of counter-regulation and its symptoms.

Eyes
A marked change in glycaemic control may cause temporary visual impairment, due to temporary alteration in the turgidity and refractive index of the lens.
Long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy. However, intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy. In patients with proliferative retinopathy, particularly if not treated with photocoagulation, severe hypoglycaemic episodes may result in transient amaurosis.

Lipodystrophy
As with any insulin therapy, lipodystrophy may occur at the injection site and delay local insulin absorption. In clinical studies, in regimens which included Lantus, lipohypertrophy was observed in 1 to 2 % of patients, whereas lipoatrophy was uncommon. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions.

Injection site and allergic reactions
In clinical studies, in regimens which included Lantus, reactions at the injection site were observed in 3 to 4 % of patients. Such reactions include redness, pain, itching, hives, swelling, or inflammation. Most minor reactions to insulins at the injection site usually resolve in a few days to a few weeks. Immediate-type allergic reactions to insulin are rare. Such reactions to insulin (including insulin glargine) or the excipients may, for example, be associated with generalised skin reactions, angio-oedema, bronchospasm, hypotension and shock, and may be life-threatening.

Other reactions
Insulin administration may cause insulin antibodies to form. In clinical studies, antibodies that cross-react with human insulin and insulin glargine were observed with the same frequency in both NPH-insulin and insulin glargine treatment groups. In rare cases, the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia. Rarely, insulin may cause sodium retention and oedema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

Storage
Store at 2 °C – 8 °C (in a refrigerator).
Keep in the outer carton.
Do not freeze. Protect from light.
Ensure that the container is not directly touching the freezer compartment or freezer packs.
Once in use, do not store above 25 °C. and keep in outer carton.

Expiry date
Do not use later than the date of expiry
Keep medicine out of the reach of children

Presentation
Solution of injection
Vial 10 ml
Box contains: 1 vial containing 10 ml solution (1000 IU). Reg. No: DKI0259201443A1

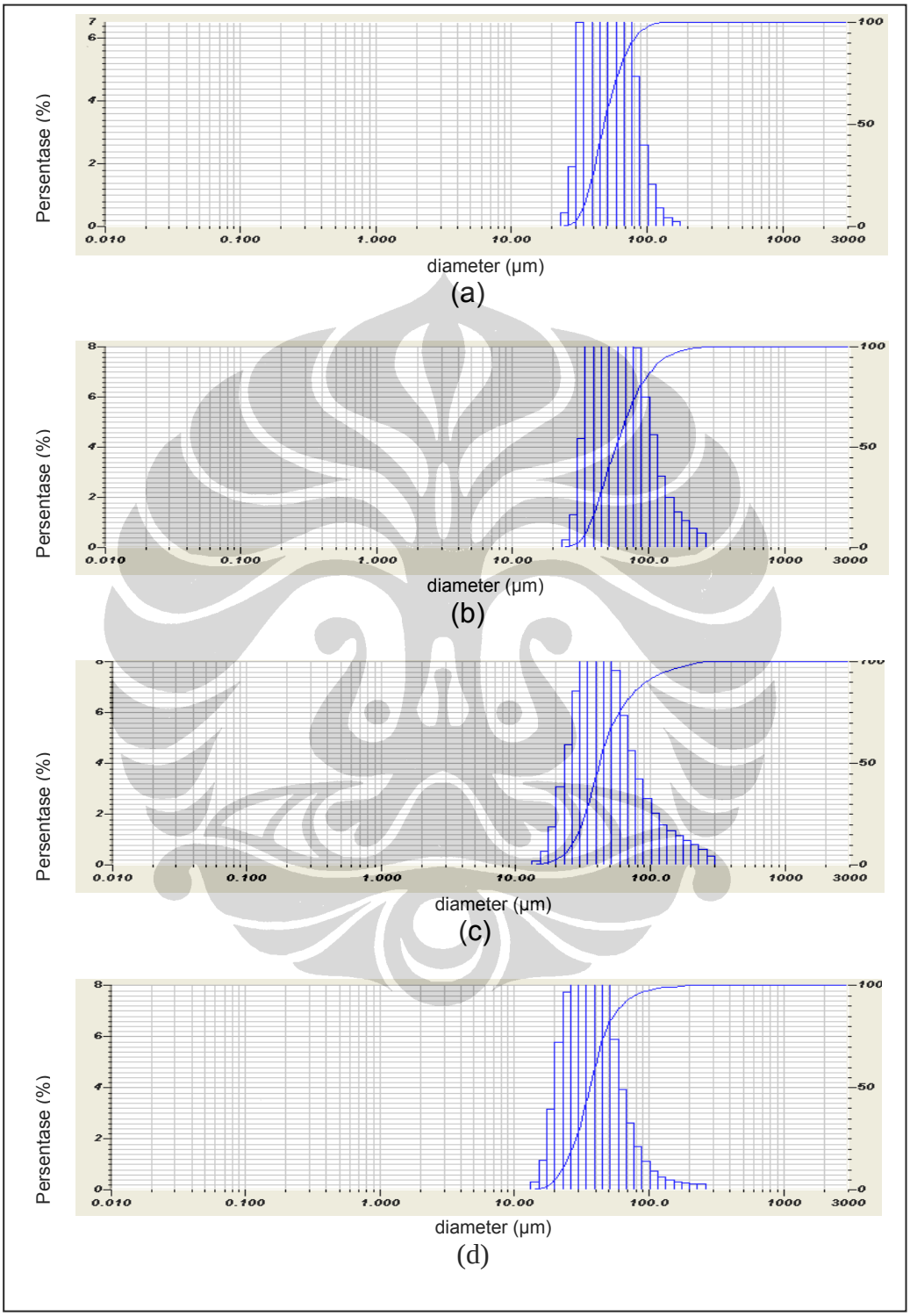
HARUS DENGAN RESEP DOKTER

ON MEDICAL PRESCRIPTION ONLY

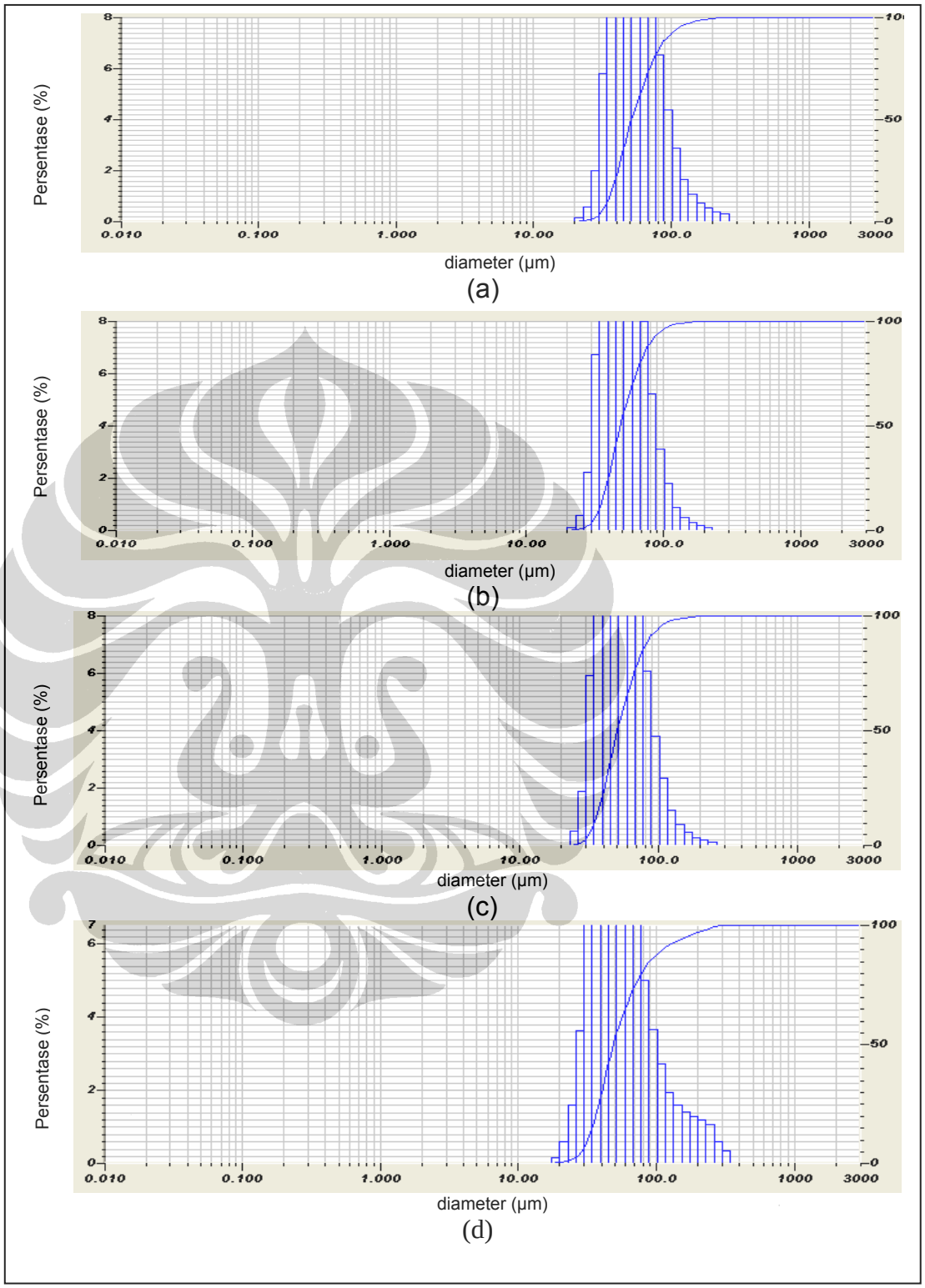
Manufactured by
Aventis Pharma Deutschland GmbH, D-65926 Frankfurt am Main, Germany.

Imported by
PT Aventis Pharma, Jakarta, Indonesia.

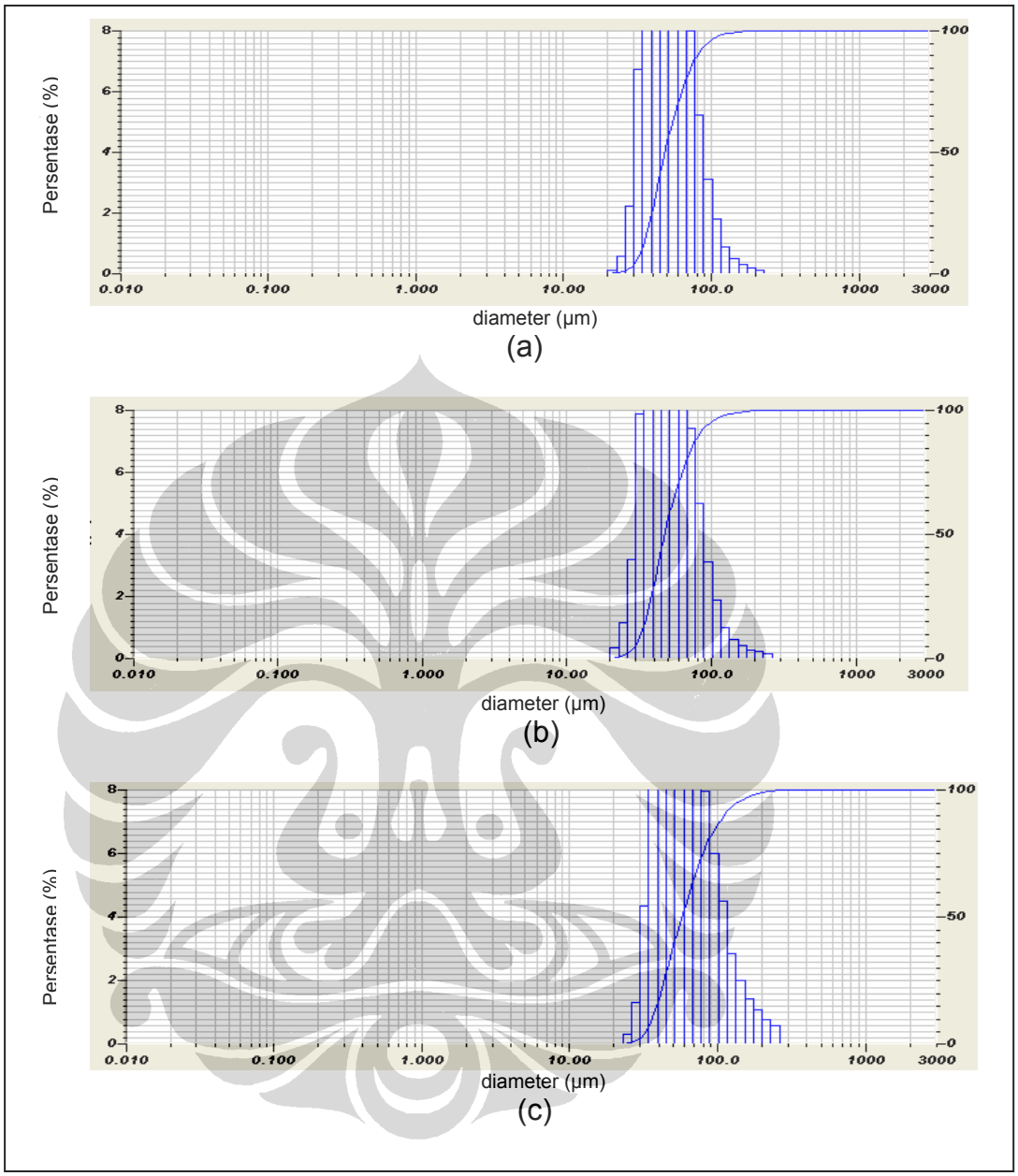
Lampiran 7
Kurva distribusi ukuran partikel



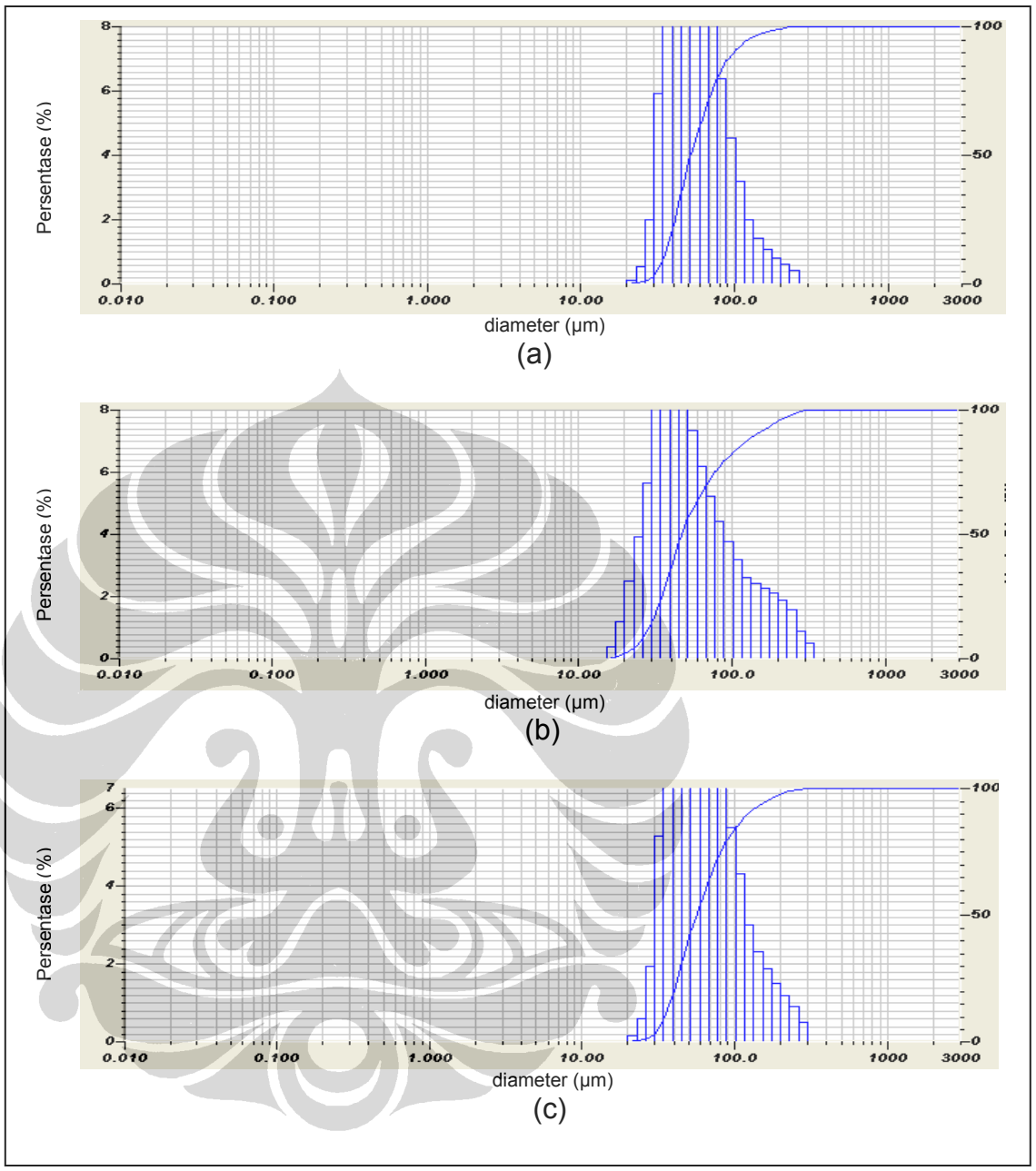
Keterangan : Kurva distribusi ukuran mikrokapsul kosong alginat. (a) alginat 2%, (b) alginat 3%, (c) alginat 4%, (d) alginat 5%.



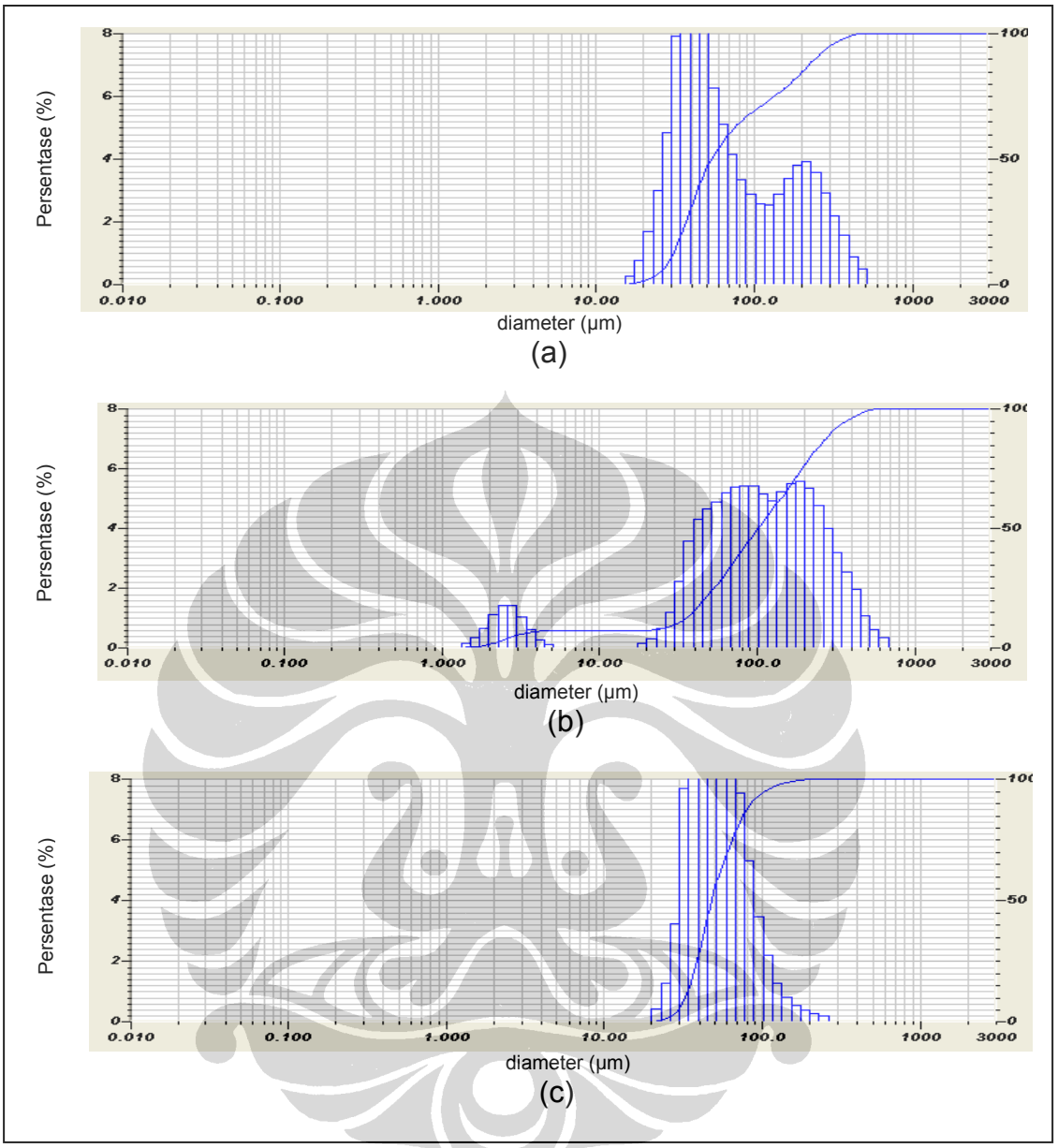
Keterangan : Kurva distribusi ukuran mikrokapsul alginat berisi BSA. (a) alginat 2%, (b) alginat 3%, (c) alginat 4%, (d) alginat 5%.



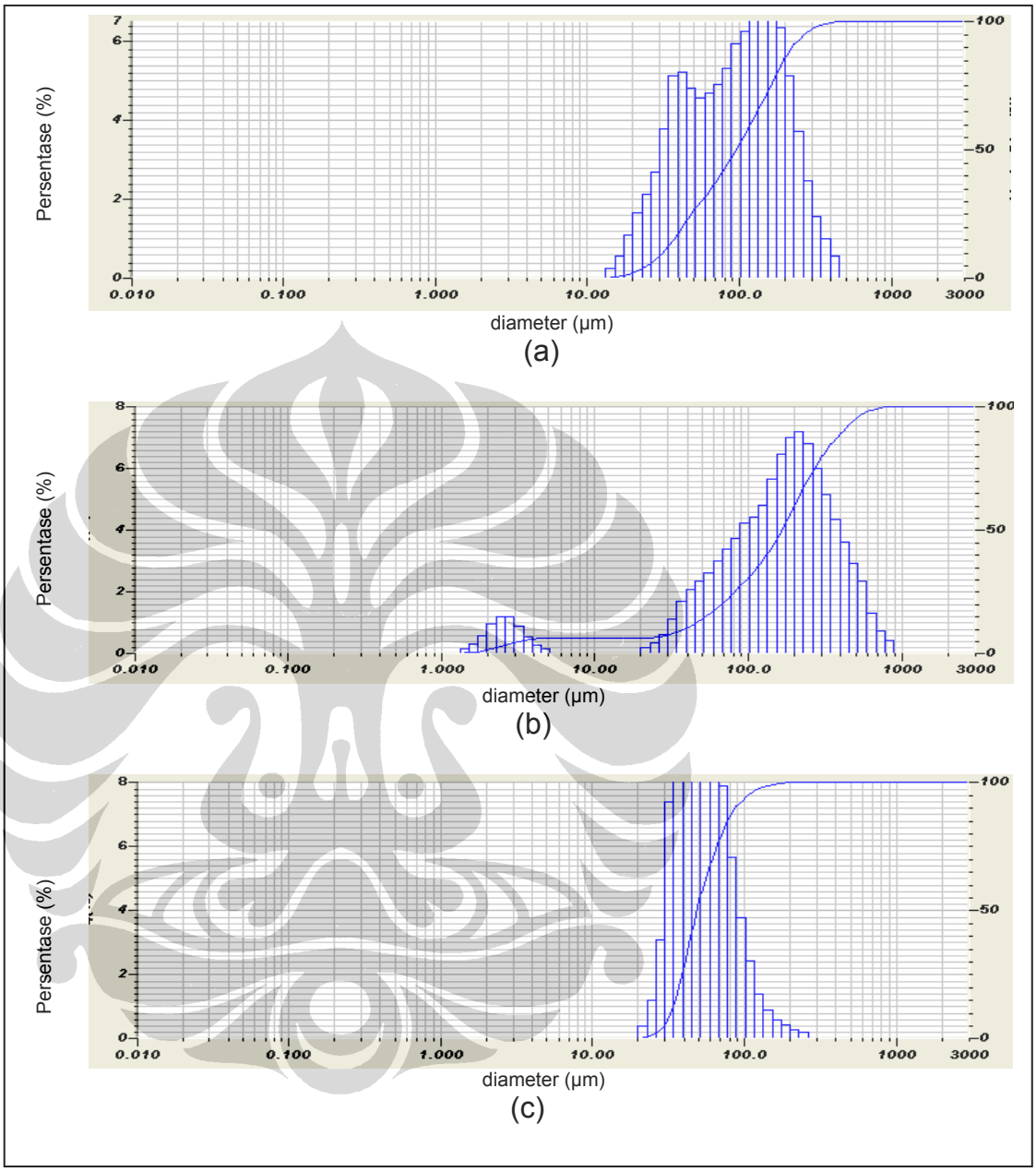
Keterangan : Kurva distribusi ukuran mikrokapsul alginat 4% berisi insulin. (a) 46,88 IU, (b) 93,75 IU, (c) 187,5 IU.



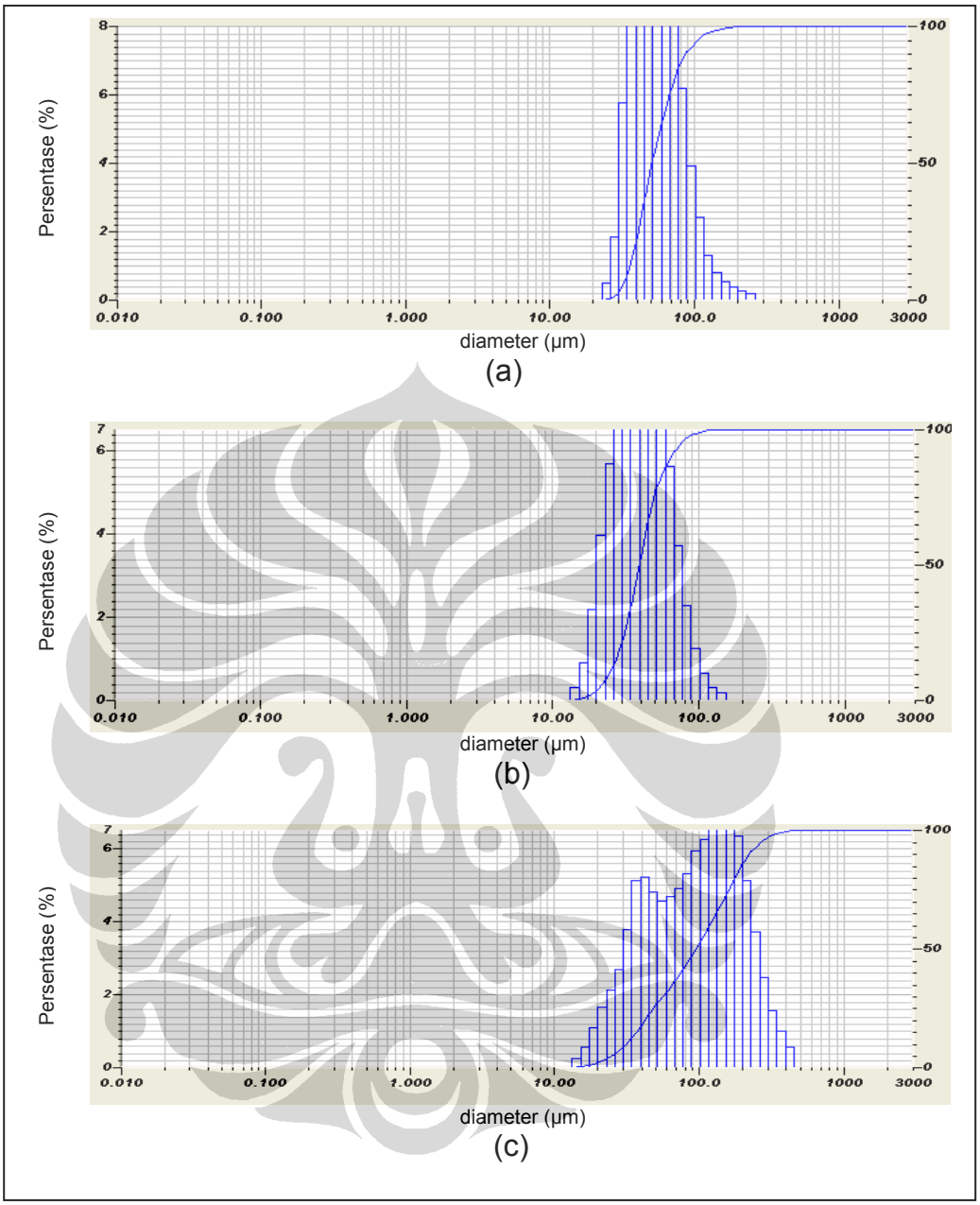
Keterangan : Kurva distribusi ukuran mikrokapsul kosong alginat 3%-kitosan. (a) kitosan 0,2%, (b) kitosan 0,3%, (c) kitosan 0,4%.



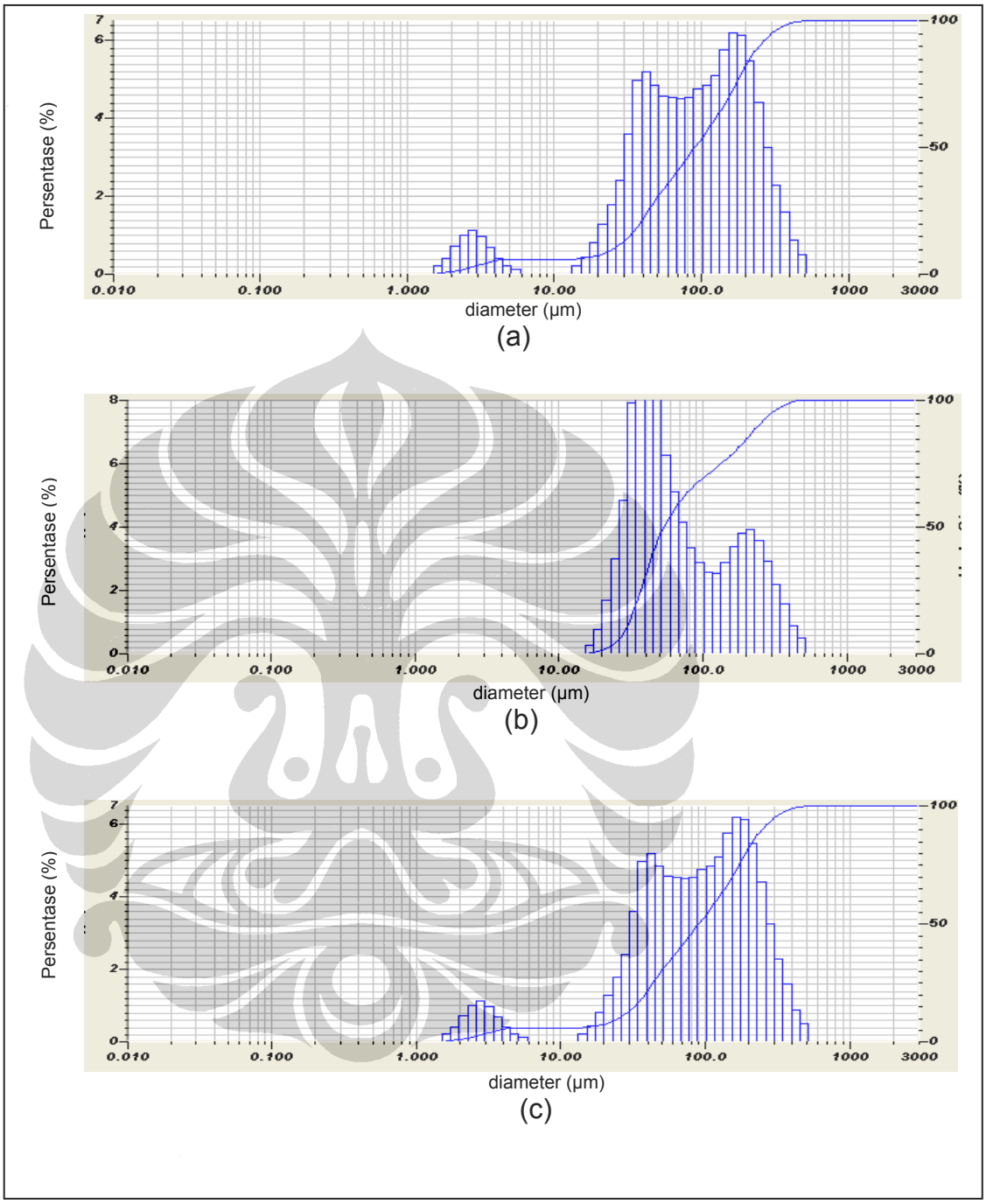
Keterangan : Kurva distribusi ukuran mikrokapsul kosong alginat 4%-kitosan. (a) kitosan 0,2%, (b) kitosan 0,3%, (c) kitosan 0,4%.



Keterangan : Kurva distribusi ukuran mikrokapsul alginat 3%-kitosan berisi BSA. (a) kitosan 0,2%, (b) kitosan 0,3%, (c) kitosan 0,4%.



Keterangan : Kurva distribusi ukuran mikrokapsul alginat 4%-kitosan berisi BSA. (a) kitosan 0,2%, (b) kitosan 0,3%, (c) kitosan 0,4%.



Keterangan : Kurva distribusi ukuran mikrokapsul alginat 4%-kitosan 0,3% berisi insulin. (a) 46,88 IU, (b) 93,75 IU, (c) 187,5 IU.