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Appendix A

The solubility of isosorbide dinitrate in various solvents.

Solvent	Sample number	Solubility (mg/ml)
reversed osmosis treated water	1	.8769
	2	.9708
	3	.9441
reversed osmosis treated water + 20% PEG400	1	1.3236
	2	1.1524
	3	1.5422
reversed osmosis treated water + 30% PEG400	1	1.6414
	2	1.7790
	3	1.3090

Appendix B

Percent water sorption of various cast films.

Formulation	Sample number	Weight of membranes (g)		% Water sorption
		before exposure to water	after exposure to water	
A2	1	.2426	.3032	24.98
	2	.2339	.2909	24.37
	3	.2314	.2952	27.57
A3	1	.2373	.3027	27.56
	2	.2310	.2828	22.42
	3	.2275	.2830	24.40
A5	1	.2161	.2582	19.48
	2	.2584	.3200	23.84
	3	.2238	.2715	21.31
A6	1	.2433	.2962	21.74
	2	.2354	.2829	20.18
	3	.2355	.2832	20.25
A8	1	.2771	.3316	19.67
	2	.2316	.2814	21.50
	3	.2576	.3075	19.37
A9	1	.2989	.3506	17.29
	2	.2474	.3003	21.38
	3	.2334	.2785	19.32
A11	1	.2621	.2922	11.48
	2	.2731	.3136	14.83
	3	.2572	.2796	8.71
A12	1	.2366	.2595	9.68
	2	.2890	.3221	11.45
	3	.2816	.3115	10.62
A14	1	.2431	.2844	16.99
	2	.2673	.3076	15.08
	3	.2267	.2513	10.85
A15	1	.2938	.3307	12.56
	2	.2450	.2728	11.35
	3	.2817	.3148	11.75
A17	1	.2247	.2380	5.92
	2	.2169	.2319	6.92
	3	.2400	.2435	1.46
A18	1	.2193	.2409	9.85
	2	.2363	.2573	8.89
	3	.2074	.2249	8.44
P3	1	.1940	.2571	32.53
	2	.1938	.2547	31.42
	3	.2063	.2781	34.80

Formulation	Sample number	Weight of membranes (g)		% Water sorption
		before exposure to water	after exposure to water	
P18	1	.2242	.2561	14.22
	2	.2039	.2318	13.68
	3	.2594	.2889	11.37
H3	1	.2435	.3319	36.30
	2	.3096	.4416	42.64
	3	.2827	.3726	31.80
H15	1	.2280	.2999	31.54
	2	.2441	.3133	28.35
	3	.2407	.3062	27.21
H18	1	.2644	.3093	16.98
	2	.2063	.2440	18.27
	3	.2596	.3065	18.07
C2	1	.2258	.2688	19.04
	2	.2504	.2869	14.58
	3	.2024	.2363	16.75
C9	1	.2439	.3079	26.24
	2	.1966	.2483	26.30
	3	.2046	.2584	26.30
C17	1	.2382	28.94	21.49
	2	.1900	.2353	23.84
	3	.2505	.3053	21.88
M2	1	28.46	.3217	13.04
	2	.3077	.3436	11.67
	3	.2250	.2474	9.96
M3	1	.2313	.2744	18.63
	2	.2344	.2840	21.16
	3	.2262	.2800	23.78
M5	1	.2688	.3251	20.94
	2	.2863	.3499	22.21
	3	.2726	.3498	28.32
M6	1	.2536	.3087	21.73
	2	.2376	.2974	25.17
	3	.1774	.2238	26.16
M9	1	.1923	.2351	22.26
	2	.2173	.2570	18.27
	3	.2563	.3093	20.68

Appendix C

Tensile test of various crosslinked chitosan-polymer membranes.

Formulation	Mean thickness (mm)	Cross section area (mm^2)	Breaking force (kg)	Ultimate tensile strength (kg/mm^2)	Elongation at break (%)
A2	.106	.6644	.2207	.3321	90
	.126	.7860	.4526	.5758	100
	.115	.7188	.2617	.3641	110
	.128	.8000	.5026	.6283	85
	.110	.6875	.4787	.6963	115
A3	.110	.6680	.3469	.5042	55
	.105	.6563	.3683	.5612	70
	.114	.7125	.4421	.6205	70
	.126	.7875	.7417	.9418	70
	.128	.8000	.8713	1.0891	70
A5	.111	.6938	.3248	.4681	100
	.121	.7536	.3750	.4958	110
	.082	.5125	.1667	.3253	100
	.096	.6000	.3350	.5583	100
	.090	.5625	.1750	.3111	110
A6	.100	.6250	.3380	.5408	65
	.099	.6188	.4395	.7102	70
	.116	.7250	.3667	.5058	65
	.096	.6000	.1817	.3028	60
	.101	.6313	.5911	.9363	70
A8	.123	.7688	.1192	.1550	65
	.096	.6000	.0964	.1607	60
	.123	.7688	.1275	.1658	65
	.101	.6313	.0709	.1123	75
	.117	.7331	.1868	.2548	90
A9	.100	.6250	.2408	.3853	65
	.123	.7688	.4398	.5721	75
	.099	.6186	.2268	.3666	60
A11	.121	.7563	.4599	.6081	60
	.107	.6688	.2365	.3536	50
	.131	.6188	.5179	.6325	65
A12	.123	.7688	.4725	.6146	30
	.105	.6563	.5221	.7955	30
	.130	.8125	.6650	.8185	40
	.102	.6375	.7903	1.2390	40
	.099	.6188	.2907	.4698	25
A14	.091	.5688	.2024	.3558	35
	.114	.7125	.3981	.5587	50
	.109	.6831	.3004	.4398	40
	.104	.6515	.1616	.2480	35
	.128	.8000	.5860	.7325	30

Formulation	Mean thickness (mm)	Cross section area (mm^2)	Breaking force (kg)	Ultimate tensile strength (kg/mm^2)	Elongation at break (%)
A15	.120	.7500	.4765	.6353	20
	.111	.6938	.4212	.6017	20
	.124	.7750	.4389	.5663	30
	.102	.6375	.5560	.8722	25
	.102	.6375	.2413	.3785	25
A17	.104	.6500	.1702	.2618	45
	.125	.7813	.2134	.2731	40
	.097	.6063	.1536	.2533	40
	.130	.8125	.2419	.2977	40
	.120	.7500	.1659	.2208	40
A18	.115	.7188	.4510	.6274	30
	.108	.6750	.3734	.5532	35
	.130	.8125	.4467	.5498	30
	.129	.8060	.2811	.3488	35
	.126	.7880	.2730	.3464	25
P3	.126	.7880	.5495	.6973	10
	.119	.7438	.5307	.7135	20
	.095	.5938	.3267	.5502	30
	.096	.6000	.5981	.9968	25
	.118	.7375	.2666	.3615	35
P18	.090	.5625	.4760	.8462	20
	.089	.5563	.4430	.7987	25
	.094	.5875	.4132	.7033	30
	.100	.6250	.3009	.4814	15
	.105	.6563	.2140	.3261	15
	.092	.5750	.2472	.4299	15
H3	.128	.8000	.6379	.7974	40
	.130	.8125	.3600	.4431	30
	.115	.7188	.4311	.5997	35
	.118	.7375	.1858	.2519	25
	.122	.7630	.6752	.8849	40
H15	.085	.5313	.4666	.8782	15
	.097	.6063	.3678	.6066	15
	.091	.5690	.3662	.6436	20
	.082	.5125	.5729	1.1179	20
	.098	.6125	.2526	.4124	20
H18	.098	.6125	.4099	.6692	20
	.127	.7938	.4403	.5547	15
	.119	.7438	.3785	.5089	10
	.111	.6938	.2215	.3193	5
	.117	.7317	.2550	.3487	15
C2	.091	.5688	.1157	.2034	20
	.112	.7000	.2642	.3774	25
	.101	.6313	.2266	.3589	30
C9	.110	.6875	.1785	.2596	25
	.102	.6375	.2553	.4005	30
	.111	.6938	.2107	.3037	30
	.099	.6188	.1227	.1983	25
	.092	.5750	.2542	.4421	35

Formulation	Mean thickness (mm)	Cross section area (mm^2)	Breaking force (kg)	Ultimate tensile strength (kg/mm^2)	Elongation at break (%)
C17	.093	.5813	.0813	.1399	15
	.110	.6880	.1635	.2376	15
	.099	.6188	.0744	.1202	10
M2	.088	.5500	.2054	.3735	35
	.104	.6500	.2693	.4143	30
	.100	.6250	.2183	.3495	30
	.104	.6500	.2185	.3362	25
	.089	.5563	.3101	.5574	30
M3	.110	.6875	.3450	.5018	10
	.129	.8063	.4282	.5311	30
	.111	.6938	.3205	.4619	30
	.100	.6250	.4617	.7387	15
	.098	.6125	.5390	.8800	25
	.129	.8063	.3439	.4265	30
	.104	.6500	.2548	.3920	30
M5	.106	.6630	.2362	.3563	25
	.139	.6688	.3197	.3680	20
	.131	.8188	.3670	.4482	20
	.115	.7188	.4021	.5594	35
	.085	.5316	.4295	.8084	40
M6	.133	.8313	.4239	.5099	25
	.116	.7250	.3495	.4821	25
	.125	.7813	.4220	.5401	30
	.118	.7375	.4693	.6363	20
	.121	.7563	.6226	.8232	15
	.105	.6563	.2583	.3936	25
M9	.103	.6438	.2252	.3498	25
	.097	.6063	.2223	.3667	25
	.094	.5875	.3522	.5995	35
	.099	.6188	.2247	.3631	25
	.112	.6700	.3326	.4751	30

Appendix D

Thickness of Various Permeated Test Membranes.

Formulation	Sample number	Thickness (mcm)				
		point 1	point 2	point 3	point 4	point 5
A11	1	106	118	111	116	103
	2	114	110	110	113	110
	3	110	120	116	117	107
A12	1	112	110	110	110	109
	2	117	107	108	110	113
	3	114	111	119	119	120
A14	1	113	111	111	115	113
	2	104	110	114	109	108
	3	116	105	110	109	117
A15	1	110	109	111	110	111
	2	115	119	113	112	114
	3	105	102	107	104	104
A17	1	109	108	110	108	107
	2	103	100	110	114	109
	3	118	112	116	118	119
A18	1	100	113	118	105	120
	2	110	118	117	117	115
	3	108	107	105	102	106
P18	1	105	98	100	109	101
	2	109	108	101	100	97
	3	102	100	103	103	108
H18	1	115	109	110	110	111
	2	111	106	103	109	105
	3	115	118	107	107	108
C2	1	100	101	117	110	120
	2	107	105	100	111	106
	3	110	111	113	110	111
M2	1	102	100	96	100	99
	2	103	100	110	102	103
	3	120	120	113	112	117

Appendix E

Cumulative amount of the ISDN permeated through shed snake skin delivered from ISDN transdermal patchs.

Formulation	Time (hours)	Cumulative drug permeated (mcg.)				
		1	2	3	Mean (SD)	
A11	0.5	-	-	-		-
	1	-	-	-		-
	2	-	-	30.9184		10.3061
	4	47.6020	27.0153	61.3287	45.3153	(17.2706)
	6	53.4638	11.4392	56.8900	40.5977	(25.3100)
	8	2.3981	.9074	19.6823	7.6626	(10.4360)
	10	28.9287	.9074	3.8970	11.2444	(15.3879)
	12	12.9838	.9074	20.7592	11.5501	(10.0033)
	16	116.1307	32.8911	43.9446	64.3221	(45.2066)
	20	180.1149	265.0168	88.8960	178.0092	(88.0793)
	24	324.6512	370.7248	126.2188	273.8649	(129.9239)
A12	0.5	20.2806	-	23.5459	14.6088	(12.7565)
	1	35.9459	-	0.5651	12.1703	(20.5922)
	2	1.3377	25.8929	19.1110	15.4472	(12.6810)
	4	26.4397	31.7438	19.7092	25.9642	(6.0314)
	6	23.9554	31.6489	38.4488	31.3510	(7.2513)
	8	38.5909	37.8859	35.9948	37.4905	(1.3424)
	10	61.9323	28.3622	62.2871	50.8605	(19.4849)
	12	66.4764	29.0995	85.3389	60.3049	(28.6231)
	16	96.5294	34.7889	163.7569	98.3584	(64.5035)
	20	194.9467	76.4675	242.9135	171.4426	(85.6761)
	24	295.8679	126.6287	264.3378	228.9448	(90.0000)
A14	0.5	24.6173	-	-		8.2058
	1	.5908	17.8571	-	6.1493	(10.1436)
	2	14.4428	23.1837	32.9337	23.5200	(9.2500)
	4	43.8569	17.6839	35.1271	32.2226	(13.3260)
	6	36.0607	1.3757	25.2625	20.8996	(17.7493)
	8	50.9865	25.6359	39.4270	38.6831	(12.6917)
	10	99.8987	37.0599	50.0403	62.3330	(33.1729)
	12	155.8244	104.1013	105.2745	121.7334	(29.5295)
	16	229.4912	193.7009	202.1135	208.4352	(18.7139)
	20	345.4519	519.3381	322.8204	395.8701	(107.5235)
	24	464.2234	634.5473	548.8964	549.2224	(85.1624)
A15	0.5	20.1020	24.1327	26.0204	23.4184	(3.0232)
	1	27.3957	24.5842	26.3388	26.1062	(1.4201)
	2	35.5161	39.9052	23.6651	33.0288	(8.4009)
	4	34.2189	28.1821	41.2441	34.8817	(6.5375)
	6	57.5479	31.0788	33.5942	40.7403	(14.6100)
	8	50.9549	42.1678	46.2993	46.4740	(4.3962)
	10	61.1873	53.6851	59.2661	58.0462	(13.8970)
	12	93.3475	90.4566	92.2388	92.0143	(1.4585)
	16	154.3598	173.4648	192.1192	173.3146	(18.8801)
	20	351.2964	254.6355	309.7704	305.2341	(48.4899)
	24	454.7081	421.9130	446.3452	440.9888	(17.0411)

Formulation	Time (hours)	Cumulative drug permeated (mcg.)			
		1	2	3	Mean (SD)
A17	0.5	46.3265	-	-	15.442
	1	20.5506	-	17.8571	12.8026 (11.1688)
	2	30.7875	-	15.6582	15.4819 (15.3945)
	4	2.2793	17.6531	20.9422	13.6247 (9.9622)
	6	2.2793	.4237	28.7778	10.5003 (15.8733)
	8	2.2793	.4237	75.6113	26.1048 (42.8839)
	10	2.2793	.4237	36.9968	13.2333 (20.6007)
	12	2.2793	.4237	38.5101	13.7377 (21.4736)
	16	46.8966	56.1635	137.1323	80.0641 (49.6392)
	20	262.8144	144.8993	195.5301	200.9479 (59.1724)
	24	292.5619	256.5999	298.8665	282.6761 (22.8016)
A18	0.5	36.7602	-	19.0051	18.5884 (18.3836)
	1	0.8822	-	22.4204	7.7675 (12.6974)
	2	29.7853	-	15.0903	14.9585 (14.8931)
	4	1.5759	-	1.3218	0.9659 (0.8461)
	6	157.7098	-	47.6738	68.4612 (80.8838)
	8	93.0328	24.3112	33.2760	50.2067 (37.3584)
	10	39.8695	33.1708	32.4604	35.1669 (4.0880)
	12	79.2227	49.1708	47.4487	58.6141 (17.8684)
	16	90.9558	108.5324	110.1781	103.2221 (10.6547)
	20	137.1641	158.6789	147.5511	147.7980 (10.7595)
	24	195.8377	243.9985	188.6686	209.5014 (30.0896)
P18	0.5	7.8316	17.7296	12.0408	12.5340 (4.9674)
	1	22.5860	24.3031	30.3145	25.7345 (4.0582)
	2	24.0164	31.2027	31.7494	28.9895 (4.3155)
	4	28.0193	16.7490	39.7576	28.1753 (11.5051)
	6	33.5844	34.3035	28.5525	32.1468 (3.1335)
	8	25.0329	32.4747	48.7657	35.4244 (12.1383)
	10	16.0284	17.8794	21.5920	18.4999 (2.8332)
	12	21.5143	36.5903	47.4900	35.1982 (13.0437)
	16	41.5888	50.0021	65.4537	52.3482 (12.1042)
	20	63.8018	99.9708	70.1912	77.9879 (19.3039)
	24	152.4931	137.4009	192.9671	160.9537 (28.7330)
H18	0.5	-	-	-	-
	1	18.0612	-	29.3112	15.7908 (14.7869)
	2	24.0559	26.1476	0.7035	16.9690 (14.1251)
	4	24.8014	35.2959	24.8872	28.3282 (6.0344)
	6	28.6379	33.8830	16.4676	26.3295 (8.9342)
	8	28.8794	2.2377	18.4489	16.5220 (13.4250)
	10	15.3355	41.5489	22.6881	26.5242 (13.5212)
	12	33.0073	43.8190	34.6722	37.1662 (5.8214)
	16	47.6012	15.6871	48.1818	37.1567 (18.5955)
	20	98.5511	41.6832	46.8502	62.3615 (31.4474)
	24	143.4588	47.0355	50.4819	80.3254 (54.7023)
C2	0.5	-	14.6172	13.6735	9.4303 (8.1805)
	1	18.9031	12.2896	29.1802	20.1243 (8.5113)
	2	17.3159	10.0761	19.5410	15.6443 (4.9489)
	4	19.7870	26.0362	11.0059	18.9430 (7.5506)
	6	34.1443	12.9658	29.0410	25.3837 (11.0528)
	8	51.3354	29.4409	21.2280	34.0014 (15.5632)
	10	57.4150	50.0548	61.4770	56.3156 (5.7899)
	12	87.6937	91.8872	83.9056	87.8288 (3.9925)
	16	158.9486	196.0993	184.7468	179.9316 (19.0377)
	20	224.3760	349.9502	356.6613	310.3292 (74.5132)
	24	578.5600	404.3891	659.8463	547.5985 (130.5126)

Formulation	Time (hours)	Cumulative drug permeated (mcg.)			
		1	2	3	Mean (SD)
M2	0.5	-	75.8928	52.0153	42.6361 (38.8061)
	1	-	39.7510	58.5188	32.7566 (29.8798)
	4	-	40.7420	36.1433	25.6284 (22.3137)
	8	29.3878	32.6491	51.3610	37.7993 (11.8574)
	12	72.3124	66.3554	56.6186	65.0955 (7.9224)
	18	138.5463	111.6703	135.9033	128.7066 (14.8130)
	24	230.0575	190.4350	209.9180	210.1368 (19.8122)

SD = Standard deviation

Appendix F

In order to quantitate the amount of ISDN that permeated from ISDN transdermal patch through shed snake skin to the receptor medium, sensitive HPLC method was used for this purpose. Chromatogram of HPLC as shown in Figures 30-31 presented the good resolution between drug and the internal standard. The run time per sample was within 12 minutes.

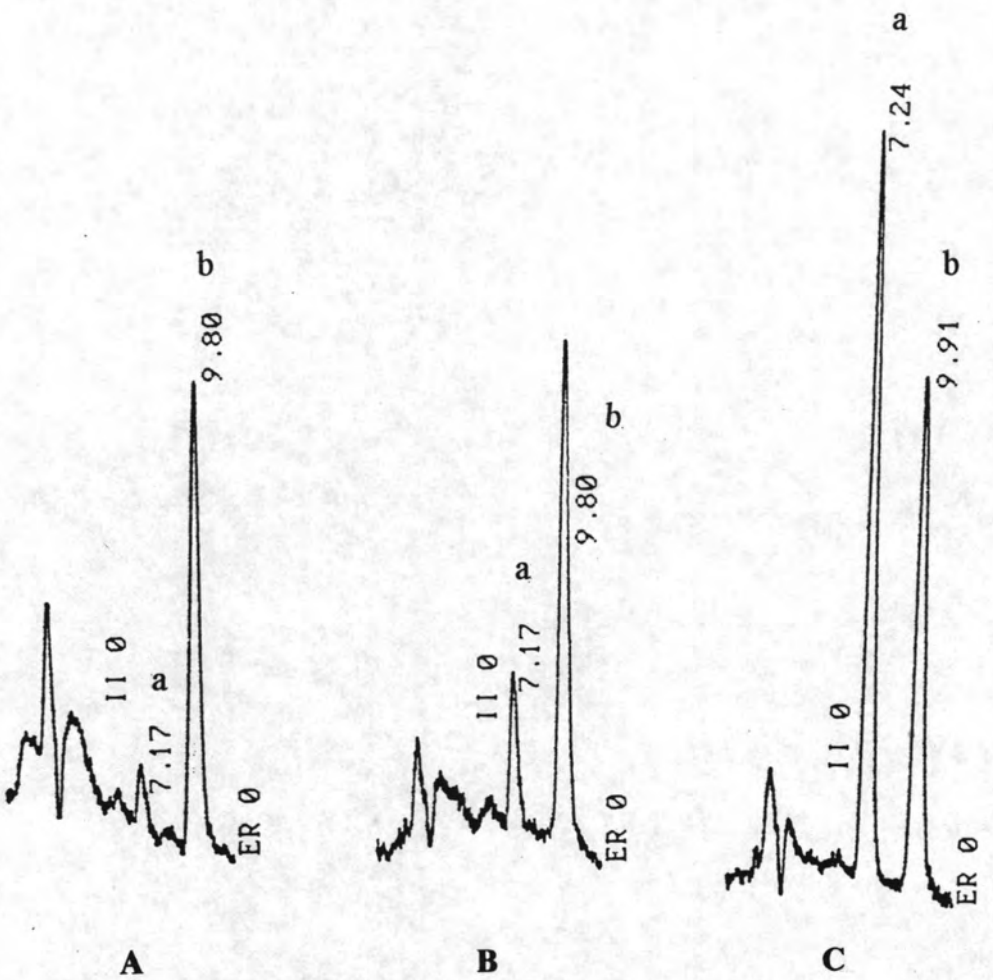

Figure 30 Typical chromatograms of some standard solutions containing of ISDN (a) and 4-Dimethylaminobenzaldehyde (b) as internal standard, A = at concentration of ISDN 0.09 μg/ml, B = at concentration of ISDN 0.2 μg/ml and C = at concentration of ISDN 1.0 μg/ml. (correlation coefficient of standard curve = 0.99495)

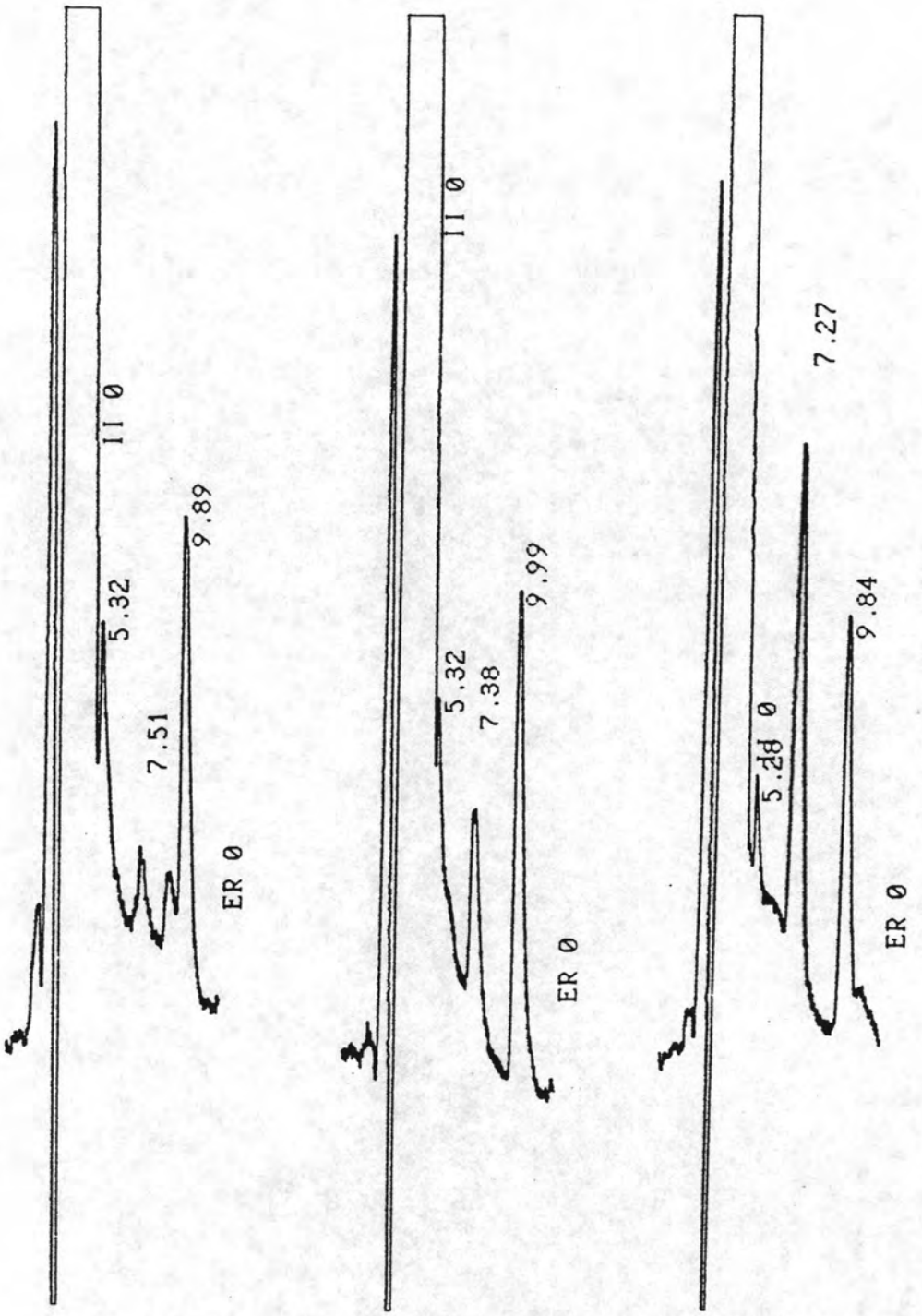

Figure 31 Chromatograms of some permeation samples containing of permeated ISDN (a) and 4-Dimethylaminobenzaldehyde (b) as internal standard.

Biography

Miss Warunee Leesajakul was born on April 7, 1966, in Bangkok. She received her degree, Bechelor of Science in Pharmacy, in 1989 from Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand.