Injectable Estradiol Vehicles and Their Compositions and Properties

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Contents

Formulations

Pharmaceutical Formulations

Medication	Brand Name(s)	Concentration and Formulation	Sources
Estradiol cypionate	Depo-Estradiol	1 mg/mL and 5 mg/mL (cottonseed oil + chlorobutanol anhydrous)	PDR (1964); FDA Label
Estradiol valerate	Delestrogen	10 mg/mL (sesame oil + 0.5% chlorobutanol)	PDR (1964); FDA Label
		20 mg/mL (castor oil + 20% benzyl benzoate + 2% benzyl alcohol)	
		40 mg/mL (castor oil + 40% benzyl benzoate + 2% benzyl alcohol)	
	Estradiol-Depot 10 mg	10 mg/mL (castor oil + benzyl benzoate)	Schug et al. (2012)
	Progynon Depot-10	10 mg/mL (castor oil + benzyl benzoate)	Schug et al. (2012)
	Neofollin	5 mg/mL (sunflower oil)	Neofollin SPC
Estradiol undecylate	Progynon Depot-100	Castor oil + 20% benzyl benzoate	Horn et al. (1993); Horn et al. (1994); Vollmer & Schneider (1996); Wünsche et al. (1998)
Estradiol valerate + norethisterone enanthate	Mesigyna	5 mg/mL EV + 50 mg/mL NETE (castor oil + benzyl benzoate 60:40)	d'Arcangues & Snow (1999)
Estradiol cypionate + medroxyprogesterone acetate	Cyclofem, Lunelle	5 mg/0.5 mL EC + 25 mg/0.5 mL MPA (microcrystalline aqueous suspension)	d'Arcangues & Snow (1999); FDA Label
Estradiol enanthate + dihydroxyprogesterone acetophenide	Deladroxate, others	10 mg EV + 150 mg DHPA (castor oil + benzyl benzoate)	Koetsawang (1994)
Estradiol valerate + hydroxyprogesterone caproate	Deluteval, Deluteval 2X	2.5 mg/mL EV + 125 mg/mL OHPC (sesame oil + 35% benzyl benzoate)	PDR (1964)

		5 mg/mL EV + 250 mg/mL (castor oil + 45% benzyl benzoate + 2% benzyl alcohol)	
Estradiol valerate + testosterone enanthate	Deladumone, Deladumone 2X	4 mg/mL EV + 90 mg/mL TE (sesame oil + 0.5% chlorobutanol)	PDR (1964)
		8 mg/mL EV + 180 mg/mL TE (sesame oil + 2% benzyl alcohol)	
Estradiol cypionate + testosterone cypionate	Depo-Testadiol	5 mg/mL EC + 50 mg/mL TC (cottonseed oil + chlorobutanol)	PDR (1964)
Estradiol valerate + prasterone enanthate	Gynodian Depot	4 mg/mL EV + 200 mg/mL prasterone enanthate (60% castor oil + 40% benzyl benzoate)	Düsterberg & Wendt (1983)

Homebrewed Formulations (As of Writing)

Medication	Brand Name	Concentration and Formulation	Sources
Estradiol valerate or estradiol enanthate	N/A (Lena's)	40 mg/mL (EV) or 50 mg/mL (EEn) (castor oil or MCT oil + "preservative (antibacterial)") [a]	lena.kiev.ua
Estradiol valerate or estradiol cypionate or estradiol enanthate	N/A (Lilian / Otokonoko Pharma's)	40 mg/mL (MCT oil + benzyl benzoate + benzyl alcohol)	Otokonoko Pharmaceuticals (EV, EC, EEn)
Estradiol valerate or estradiol cypionate or estradiol enanthate	N/A	40 mg/mL (MCT oil + benzyl benzoate + benzyl alcohol)	Onnanoko Pharma (EV, EC, EEn)

[a] Used to also provide grape seed oil but no longer does so.

Oils and Compositions

Oil	Composition	Source(s)
Sesame oil	• Linoleic acid [C18] (41%) • Oleic acid [C18] (39%) • Palmitic acid [C16] (8%) • Stearic acid [C18] (5%)	Wiki; Ghazani & Marangoni, 2016
Castor oil	• Ricinoleic acid [C18] (85–95%) • Oleic acid [C18] (2–6%) • Linoleic acid [C18] (1–5%)	Wiki
Cottonseed oil	• Linoleic acid [C18] (54%) • Palmitic acid [C16] (22%) • Oleic acid [C18] (20%)	Ghazani & Marangoni, 2016
Peanut oil (arachis oil)	• Oleic acid [C18] (45–53%) • Linoleic acid [C18] (27–32%) • Palmitic acid [C16] (11–14%) • Other (3–9%)	Ghazani & Marangoni, 2016; Wiki
Ethyl oleate	• Ethyl oleate [a] [C20] (100%)	Wiki
Grape seed oil	• Linoleic acid [C18] (70%) • Oleic acid [C18] (16%) • Palmitic acid [C16] (7%) • Stearic acid [C18] (4%)	Wiki
Tea seed oil	• Oleic acid [C18] (76–82%) • Linoleic acid [C18] (5–11%) • Palmitic acid [C16] (7.5–10%) • Stearic acid [C18] (1.5–3%)	Wiki
Sunflower oil [b]	• Linoleic acid [C18] (59%) • Oleic acid [C18] (30%) • Stearic acid [C18] (6%) • Palmitic acid [C16] (5%)	Wiki
MCT oil	• “MCT oil contains 100% MCTs, making it a concentrated source” • “It’s made by refining raw coconut or palm oil to remove other compounds and concentrate the MCTs naturally found in the oils” • “Here are the four types of MCTs, listed in order of fatty acid chain length, from shortest to longest: caproic acid [C6], caprylic acid [C8], capric acid [C10], lauric acid [C12]” • “MCT oils generally contain 50–80% caprylic acid [C8] and 20–50% caproic acid [C6]”	Healthline

Coconut oil	• Lauric acid [C12] (48%) • Myristic acid [C12] (16%) • Palmitic acid [C16] (10%) • Capric acid [C10] (8%) • Caprylic acid [C8] (7%) • Oleic acid [C18] (7%) • Other (5%)	Wiki
Palm oil	• Palmitic acid [C16] (44%) • Oleic acid [C18] (37%) • Linoleic acid [C18] (9%) • Stearic acid [C18] (4%) • Myristic acid [C12] (1%) • Others (6%)	Wiki
Viscoleo (fractionated coconut oil / MCT oil) [c]	• Caprylic acid [C8] (55–58%) • Capric acid [C10] (40%) • Lauric acid [C12] (1–5%) • Caproic acid [C6] (0.5%)	Wiki

[a] Ethyl oleate = oleic acid and ethanol ester.

[b] But different varieties with differing compositions... (high-linoleic, high-oleic, mid-oleic, high-stearic).

[c] Used in many depot injectable antipsychotic formulations (Wiki-Table).

Fat Lipophilicity (Log P)

Oils

- Castor oil: 17.8 (XLogP3-AA) (PubChem)
  - "[Castor oil] is a mixture of glycerides, chiefly ricinolein (the glyceride of ricinoleic acid)."
  - Ricinolein = triricinolein -> XLogP3-AA = 17.8 (~3x that of ricinoleic acid) (PubChem)

Triglycerides

Triglyceride	FA Carbons [a]	Log P [a]	P [b]	Source
Trilinolein	C18	20.3	2.00e+20	PubChem
Triolein	C18	22.4–23	2.51e+22–1.0e+23	PubChem
Tripalmitin	C16	21.9	7.94e+21	PubChem
Tristearin	C18	24–25.2	1e+24–1.58e+25	PubChem
Triricinolein	C18	17.8	6.31e+17	PubChem
Trimyristin	C12	16.3–18.7	2.00e+16–5.01e+18	PubChem

Trilaurin	C12	15.4	2.51e+15	PubChem
Tricaprin	C10	12.2	1.58e+12	PubChem
Tricaprylin	C8	8.9–9.2	7.9e+8–1.5e+9	PubChem
Tricaproin	C6	5.7	5e+5	PubChem

[a] Fatty acid carbons.

[b] XLogP3 in most cases. P = [Octanol/water] partition coefficient.

Fatty Acids

Fatty Acid	Carbons	Log P [a]	P [a]	Source
Linoleic acid	C18	6.8–7.05	6.3e+6–1.12e+7	PubChem
Oleic acid	C18	6.5–7.73	3.2e+6–5.37e+7	PubChem
Palmitic acid	C16	5.31–7.17	2.04e+5–1.48e+7	PubChem
Stearic acid	C18	7.4–8.23	2.5e+7–1.7e+8	PubChem
Ricinoleic acid	C18	5.7–6.19	5e+5–1.55e+6	PubChem
Myristic acid	C12	5.3–6.11	2e+5–1.29e+6	PubChem
Lauric acid	C12	4.2–4.6	1.6e+4–4e+4	PubChem
Capric acid	C10	4.09–4.1	1.23e+4–1.3e+4	PubChem
Caprylic acid	C8	3.0–3.05	1e+3–1.12e+3	PubChem
Caproic acid	C6	1.88–1.92	7.59e+1–8.32e+1	PubChem
Ethyl oleate [b]	C20	8.0	1e+8	PubChem

[a] XLogP3 in most cases. P = [Octanol/water] partition coefficient.

[b] Oleic acid ethyl ester.

Oil Viscosity

Florence (2010)

Florence, A. T. (2010). Looking at Formulations. In Florence, A. T. *An Introduction to Clinical Pharmaceutics* (pp. 69–100). Pharmaceutical Press. [Google Scholar] [Google Books]:

Table 4.3: Viscosity of oils used in depot injections.

Oil	Viscosity (cP)
Ethyl oleate	5.9
Viscoleo	12
Sesame oil	33
Arachis oil	35.2
Peanut oil	38
Castor oil	283
Viscoleo/sesame 50:50	23
Viscoleo/castor oil 75:25	27
Sesame/castor oil 50:50	55

Larsen, Thing, & Larsen (2012)

Larsen, S. W., Thing, M. A., & Larsen, C. (2012). Oily (lipophilic) solutions and suspensions. In *Long Acting Injections and Implants* (pp. 113–135). Springer, Boston, MA. [DOI:10.1007/978-1-4614-0554-2_7]:

Table 7.3: Chemical composition, density, and viscosity of commonly used vegetable oils applied for parenteral drug delivery.

Oil	Composition		Density (g/mL)	Viscosity (mPa•s)
Castor oil (ricinus oil)	C16	1%	0.957–0.965	283 (37°C)
	C18	1%		
	C18:1	3%		
	C18:2	4%		
	C18:1 (OH)	90%		
	Other fatty acids	1%		
Corn oil	C16	13%	0.917–0.925	37–39
	C18	3%		
	C18:1	31%		
	C18:2	52%		
	C18:3	1%		
	Other fatty acids	1%		
Cottonseed oil	C16	24%	0.918–0.926	70 (20°C)

	C18	3%		
	C18:1	19%		
	C18:2	53%		
	Other fatty acids	2%		
Medium-chain triglyceride (MCT, fractionated coconut oil, Viscoleo®, Miglyol 812®)	C8	~60%	0.942	12 (37°C) 23 (25°C)
	C10	~40%		
Olive oil	C16	10%	0.910–0.916	36 (40°C) 84 (20°C)
	C18	2%		
	C18:1	78%		
	C18:2	7%		
	Other fatty acids	2.0%		
Peanut oil, groundnut oil, arachis oil	C16	13%	0.914–0.917	35–38 (37°C)
	C18	23%		
	C20	1%		
	C22	3%		
	C24	2%		
	C18:1	37%		
	C18:2	41%		
	Other fatty acids	2%		
Sesame oil	C16	9%	0.915–0.923	33 (37°C) 56 (25°C)
	C18	6%		
	C18:1	38%		
	C18:2	45%		
	Other fatty acids	2%		
Soybean oil	C16	11%	0.919–0.925	50 (25°C) 69 (20°C)
	C18	4%		
	C20	1%		
	C18:1	22%		

	C18:2	53%		
	C18:3	8%		
	C20:1	1%		
	Other fatty acids	1%		

[a] Composition of the fatty acids in the triglycerides; C8=caprylic acid, C10=capric acid, C16=palmitic acid, C18=stearic acid, C20=arachidic acid, C22=behenic acid, C24=lignoceric acid, C18:1=oleic acid, C18:2=linoleic acid, C18:3=linolenic acid, C18:1 (OH)=ricinoleic acid, C20:1=eicosenoic acid.

Basco USA

Basco USA. Viscosity Charts & Conversion Tables. [PDF]:

Oil	**Absolute Viscosity (cP)**	**Temp. °F (°C)**
Castor oil	580	80 (27)
	36	175 (79.4)
Coconut oil	55	75 (24)
	30	100 (37.8)
Corn oil	28	135 (57.2)
Cottonseed oil	62	75 (24)
	24	125 (51.7)
Palm oil	43	100 (37.8)
Peanut oil	38	100 (37.8)

Diamante & Lan (2014)

Diamante, L. M., & Lan, T. (2014). Absolute viscosities of vegetable oils at different temperatures and shear rate range of 64.5 to 4835 s^{-1}. *Journal of Food Processing*, *2014*. [DOI:10.1155/2014/234583]:

Table 2: Mean and standard error for absolute viscosity of the different vegetable oils at different temperatures for a shear rate range of 64.5 to 4835 s^{-1} and the coefficients of determination (r^2) of linear regression for the shear stress and shear rate data.

Oil	**Temperature (°C)**	**Absolute viscosity (Pa•s)**	r^2
Avocado	26	0.0576 ± 0.0002	0.9996–1.0000
	38	0.0364 ± 0.0003	0.9996–1.0000

	50	0.0287 ± 0.0006	0.9997–1.0000
Canola	30	0.0462 ± 0.0005	0.9997–1.0000
	50	0.0245 ± 0.0002	0.9993–0.9998
	90	0.0108 ± 0.0004	0.9952–0.9982
Grapeseed	26	0.0466 ± 0.0003	0.9997–1.0000
	38	0.0311 ± 0.0001	0.9999–1.0000
	50	0.0227 ± 0.0000	0.9995–1.0000
Macadamia nut	26	0.0583 ± 0.0003	0.9998–0.9998
	38	0.0394 ± 0.0002	0.9816–1.0000
	50	0.0272 ± 0.0012	0.9997–0.9998
Olive	26	0.0562 ± 0.0003	0.9997–1.0000
	38	0.0341 ± 0.0005	0.9994–1.0000
	50	0.0261 ± 0.0003	0.9997–1.0000
	70	0.0157 ± 0.0001	0.9990–0.9992
Peanut	26	0.0574 ± 0.0007	0.9992–0.9996
	38	0.0380 ± 0.0002	0.9999–1.0000
	54	0.0236 ± 0.0003	0.9998–0.9999
Rapeseed	26	0.0592 ± 0.0011	0.9998–0.9999
	38	0.0376 ± 0.0001	1.0000–1.0000
	50	0.0305 ± 0.0001	0.9972–0.9998
Rice bran	26	0.0593 ± 0.0006	0.9996–0.9997
	38	0.0398 ± 0.0001	0.9999–1.0000
	50	0.0280 ± 0.0000	0.9997–0.9999
Safflower	26	0.0445 ± 0.0003	0.9998–1.0000
	38	0.0299 ± 0.0000	0.9989–1.0000
	50	0.0239 ± 0.0005	0.9992–0.9996
Sesame	26	0.0525 ± 0.0007	0.9999–0.9999
	38	0.0351 ± 0.0002	1.0000–1.0000
	50	0.0251 ± 0.0002	0.9995–0.9999

Soybean	30	0.0405 ± 0.0003	0.9993–1.0000
	50	0.0232 ± 0.0001	0.9996–0.9998
	90	0.0098 ± 0.0003	0.9905–0.9980
Sunflower	26	0.0488 ± 0.0002	0.9998–0.9999
	38	0.0323 ± 0.0005	0.9998–0.9999
	50	0.0234 ± 0.0001	0.9975–0.9993
Walnut	26	0.0429 ± 0.0003	0.9998–0.9999
	38	0.0296 ± 0.0002	0.9989–1.0000
	50	0.0212 ± 0.0001	0.9975–0.9972

Table 3: Absolute viscosities of the different vegetable oils at different temperatures (experimental and published).

Oil	**Temperature (°C)**	**Absolute viscosity (Pa•s)**			
		Experimental*	**Published Ref1**	**Published Ref2**	**Published Ref3**
Olive	40	0.0341	0.0363		0.0463 (35°C)
	70	0.0157	0.0124		0.0181 (65°C)
Peanut	26	0.0574	0.0565 (21°C)		
	38	0.0380	0.0387		0.0456 (35°C)
	54	0.0236	0.0268		0.0275 (50°C)
Rapeseed	38	0.0376		0.0449	
	50	0.0305		0.0303 (49°C)	
Safflower	26	0.0445	0.0522 (25°C)		
	38	0.0299	0.0286		0.0353 (35°C)
Sesame	38	0.0351	0.0324		0.0411 (35°C)
	50	0.0251			0.0248
Soybean	30	0.0405	0.0406		0.0386 (35°C)
	50	0.0232	0.0206	0.0233 (49°C)	0.0236
	90	0.0098	0.0078	0.0095 (82°C)	0.0087 (95°C)
Sunflower	38	0.0323	0.0311		
	50	0.0234			0.0250

* Mean of 3 measurements; Ref1: Steffe [12]; Ref2: Noureddini et al. [13]; Ref3: Fasina and Colley [9].

Akhtar et al. (2009)

Akhtar, N., Adnan, Q., Ahmad, M., Mehmood, A., & Farzana, K. (2009). Rheological studies and characterization of different oils. *Journal of the Chemical society of Pakistan*, *31*(2), 201–206. [URL] [PDF]:

Table 4: Average values of different parameters of different oils.

Oil	**Viscosity (mPs•s)**
Olive oil	63.61
Coconut oil	44.16
Almond oil	65.68
Castor oil	686.24
Sesame oil	54.37
Cottonseed oil	58.24
Sunflower oil	58.19