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APPENDIX

Witepsol can be divided into four Series.

2.1 WITEPSOL Series H is an accordance with the specifications for A deps solidus official in the Third Supplement to Sixth Edition to the German Pharmacopoeia. It is mainly used for the industrial mass production of Suppositories.

A feature of practical interest, and at the same time one of the greatest advantages of these suppository compounds compared with Oleum Cocao, is the small interval between meting point and solidification point. WITEPSOL Series H should not be ice-cooled as this will cause the formation of a rapidly solidifying outer jacket around a somewhat more slowly solidifying core, which may cause loss through breakage.

WITEPLOL H 12 A suppository compound with low melting point, suitable, inter alia, for use with drugs which greatly increase the stability of suppositories.

WITEPSOL H 15 A universally applicable suppository compound, particularly well suited for industrial mass production.

WITEPSOL H 19 A special compound containing a skin preservative which forms a film, wetting and protecting the mucous membranes.

2.2 Witepsol Series W can be used for industrial production also by means of automatic casting machines as well as for manufacture in dispensaries. With this excipient, the compound can be poured directly into the mould, cooled by ice or otherwise, without difficulty and without the risk of brittleness.

WITEPSOL W 25 A universally applicable suppository compound for industrial mass production in casting machines.

WITEPSOL W31 A universally applicable suppository compound specially suited for industrial production in casting machines.

WITEPSOL W 35 A universally applicable suppository compound, particularly well suited for extreme cooling conditions (ice cooling) in industry and dispensaries.

WIPETSOL W45 A universally applicable suppository compound, particularly well suited for small - scale - manufacture in dispensaries

2.3 WITEPSOL Series S is a special type designed for industrial mass production. It is distinguished by an extremely good dispersing capacity for drugs of particularly high density.

WITEPSOL S 52 A special compound with low melting point and enhanced dispersing capacity for use with drugs which greatly increase the stability of suppositories.

WITEPSOL S 55 A special compound with enhanced dispersing capacity, particularly well suited for use with drugs of comparatively high density, and for the manufacture of vaginal suppositories and pessaries.

WITEPSOL S 58 A special compound with low melting point, containing a special preservative, particularly well suited for the manufacture of vaginal suppositories.

2.4 WITEPSOL Series E is a special compound with a melting point above body temperature. It is used wherever it is intended to incorporate drugs which have the effect of greatly lowering the melting point. (open tube)

WITEPSOL Series E can be mixed with all other types of WITERSOL in any proportion.

WITEPSOL E 75 A special compound with higher melting point for use with ingredients which tend to lower the melting point slightly.

WITEPSOL E 76 A special compound with higher melting point for the industrial production of suppositories in casting machines.

WITEPSOL E 79 A special compound with higher melting point containing a preservative.

WITEPSOL E 85 A special compound with exceptionally high melting point which can be used for adjusting the melting point of suppositories (8)

Table 1 Chemical and Physical Characteristic of Wilepsol H,W.

WITEPSOL	H 12	H 15	H 19	W 25	W 31	W 35	W 45
Melting point (°C) (open-tube melting point)	32 - 33.5	33.5-35.5	33.5-35.5	33.5-35.5	35-37	33.5-35.5	33.5-35.5
Solidification point (°C) (Shukoff method)	29 - 32	32.5-34.5	29-32	27-30	30-32	27-30	29-32
Colour number	elow 3	below 3	below 3	below 5	below 5	below 3	below 3
Acid number	elow 0.2	elow 0.2	below0.2	below0.3	below0.3	below0.3	below0.3
ification number	240-245	230-240	230-240	225-240	225-235	225-235	225-235
Iodine number (Kaufmann)	below 3	below 3	below 7	below 3	below 3	below 3	below 3
Hydroxyl number	below 15	below 15	25-35	ca.30	below30	40-50	40-50
Unsaponifiable matter (petroleum ether method)	below 0.3	below 0.3	below0.3	below 0.3	below 0.5	below 0.3	below 0.3

Table 2 Chemical and Physical Characteristic of Witepsol S.E.

WITEPSOL	S 52	S 55	S 58	E 75	E 76	E 79	E 85
Melting Point (°C) (open-tube melting point)	32-33.5	33.5-35.5	32-33.5	37-39	37-39	36-38	42-44
Solidification Point (°C) (Shukoff method)	27-30	29-32	29-29	32-36	32-34	33-35	36-38
Colour number	below 3	below 3	below 3	below 3	below 3	below 3	below 3
Acid number	below 1	below 1	below 1	below 1,3	below 1	below 1	below 1
Saponification number	220-230	220-230	ca.220	220-230	220-230	220-230	220-230
Iodine number (Kaufmann)	below 3	below 3	below 7	below 3	below 3	below 7	below 3
Hydroxyl number	50-65	50-65	ca.75	below 15	30-40	25-35	below 15
Unsaponifiable matter (petroleum ether method)	below 2	below 2	below 2	below 3	below0.5	below 3	below 0.5

LUBRICATION OF MOLD

Lubricating the cavities of the mold is helpful in producing elegant cocoa-butter suppositories free from surface depressions.

The lubricant must be different in nature from the suppository mass, otherwise it will become absorbed, and fail to provide a buffer film between the mass and the metal. Consequently, on oily lubricant is useless for cocoa butter suppositories : for these the following has been found satisfactory:-

Soft Soap		
Glycerin ----------	of each	1 part
Alcohol (90%)		5 parts

This lubricant would, for the reason noted above, be quite unsuitable for use with a gelato-glycerin mass, and for this it is necessary to use an oil, e.g. liquid paraffin, olive, or almond oil.

Carbowax(R). Nycoline; macrogol; Solbase; polyethylene glycol PEG. Solid and liquid polyithylene glycols of the general formula

$$HOCH_2 (CH_2O\ CH_2)_x\ CH_2OH$$

Carbowax 4000. Average mol. wt 3000-3700. Hard, white,waxy solid. Solidifying range 50-55°. Solubility in water at 20° approx 62% w/w. Insoluble in petrolium ether.

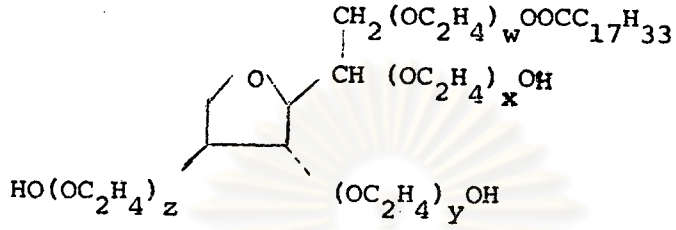
Carbowax 1540. Average mol wt 1300-1600. Soft, white waxy solid. Solidifying range 40-50°. Solubility in water at 20° approx 70% w/w. Insoluble in petrolium ether. (14)

Tween 20 (Polyoxyethylene sorbitan monolaurate) is a yellow oily liquid at 25°C.

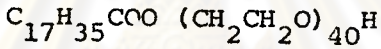
Tween 40 (Polyoxyethylene sorbitan monopalmitate) is a yellow oily liquid at 25°C.

Tween 60 (Polyoxyethylene sorbitan monostearate) is a yellow oily liquid at 25°C.

Tween 80 Polyoxyethylene (20) sorbitan monooleate is sorbitan ester. It derived from esters of sorbitol and it anhydrides copolymerized with a varying number of moles of ethylene oxide.



Myrj 52 Polyoxy (40) stearate is a mixture of the monostearate and distearate of mixed polyoxyethylene diols and the corresponding free glycols the average polymer length being equivalent at about 40 (U.S.P) or 50 (N.F) oxyethylene units. (10)



Borate buffer solution pH, 10.0 contains: (11)

Sodium borate	11.25	g
1 N Sodium hydroxide	41.0	ml
Distilled water to	1,000	ml

Table 3. Releasing time and concentration of Phenobarbital from Various suppository bases

	Witepsol E 85 + Phenobarbital 250 mg.				
Time (min)	10	30	60	90	120
Av. conc.(mg/ml)	0	0	0.01	.02	0.06
	Witepsol S 55 + Phenobarbital 250 mg.				
Time (min)	10	30	60	90	120
Av. conc.(mg/ml)	0.02	0.02	0.04	0.08	0.10
	Concoa butter 90% + White Beeswax 10% + Phenobarbital 250 mg.				
Time (min)	10	30	60	90	120
Av. conc.(mg/ml)	0.02	0.03	0.05	0.06	0.08
	PEG 4000, 60% + PEG 1500, 40% + Phenobarb 250 mg.				
Time (min)	10	20	30	38	
Av. conc.(mg/ml)	0.38	0.69	0.88	0.95	

Table 4. Releasing time and Concentration of Phenobarbital from different Combinations of PEG bases

	PEG 400, 25% + PEG 1500,75% + Phenobarbital			
Time (min)	10	20	30	40
Av.Conc.(mg/ml.)	0.40	0.64	0.90	0.93
	PEG 4000,30% +PEG 1500,70% + Phenobarb 250 mg.			
Time (min)	10	20	30	40
Av.Conc.(mg/ml.)	0.41	0.70	0.86	0.93
	PEG 4000,40% + PEG 1500,60% + Phenobarb 250 mg.			
Time (min)	10	20	30	39.15
Av.Conc.(mg/ml)	0.42	0.69	0.88	0.98
	PEG 4000,50% + PEG 1500,50% +Phenobarb 250 mg.			
Time(min)	10	20	30	39
Av.Conc.(mg/ml.)	0.37	0.66	0.85	0.96
	PEG 4000, 60% + PEG 1500, 40%+ Phenobarb 250 mg.			
Time (min)	10	20	30	38
Av.Conc(mg/ml.)	0.38	0.69	0.88	0.95
	PEG 4000,70% + PEG 1500, 30% + Phenobarb 250 mg.			
Time (min)	10	20	30	41
Av.Conc.(mg/ml)	0.36	0.61	0.82	0.95
	PEG 4000,47% + PEG 1500,33% + PEG 400,20% + Phenobarb 250 mg.			
Time (min)	10	20	30	38
Av.Conc.(mg/ml.)	0.35	0.67	0.89	0.97

Table 5. Releasing time and Concentration of Phenobarbital from different combinations of PEG bases and Tween 20.

	PEG 4,000,60% + PEG 1500, 40% + Phenobarb 250 mg.			
Time (min)	10	20	30	38
Av. Conc(mg/ml)	0.38	0.69	0.88	0.95
	PEG 4000,58% + PEG 1,500,40% + Tween 20, 2%+Phenobarb 250 mg.			
Time (min)	10	20	30	38.45
Av.Conc(mg/ml.)	0.36	0.65	0.87	0.91
	PEG 4,000,55% + PEG 1,500,40 % + Tween 20,5% + Phenobarb 250 mg.			
Time (min)	10	20	30	38.45
Av.Conc(mg/ml.)	0.35	0.63	0.84	0.94

Table 6. Releasing time and concentration of Phenobarbital from different Combinations of PEG bases and Tween 40

	PEG 4,000,60%+ PEG 1,500.40% + Phenobarb 250 mg.			
Time (min)	10	20	30	38
Av.Conc(mg/ml.)	0.38	0.69	0.88	0.95
	PEG 4,000.55%+ PEG 1,500.40% + Tween 40,5% +Phenobarb 250mg.			
Time (min)	10	20	30	44.45
Av.Conc.(mg/ml.)	0.31	0.56	0.77	0.95
	PEG 4,000.50% + PEG 1,500.40%+Tween 40,10%+Phenobarb 250 mg.			
Time (min)	10	20	30	37
Av.Conc..(mg/ml.)	0.31	0.57	0.75	0.82
	PEG 4,000.45% + PEG 1500,40% +Tween 40,15% + Phenobarb 250mg			
Time (min)	10	20	30	39.40
Av.Conc(mg/ml)	0.31	0.56	0.75	0.87
	PEG 4000,60%+PEG 1500,35%+Tween 40,5%+Phenobarb 250 mg.			
Time (min)	10	20	30	41.30
Av.Conc(mg/ml.)	0.33	0.61	0.82	0.95
	PEG 4000,60%+PEG 1500,30% +Tween 40,10% +Phenobarb 250 mg.			
Time (min)	10	20	30	39.15
Av.Conc. (mg/ml)	0.34	0.61	0.80	0.89
	PEG 4000,60%+PEG 1500,25%+Tween 40,15%+Phenobarb 250 mg.			
Time (min)	10	20	30	38.37
Av.Conc..(mg/ml.)	0.33	0.62	0.84	0.90

Table 7. Releasing time and concentration of Phenobarbital from different combinations of PEG bases and Tween 60

	PEG 4000,60%+PEG 1500,40%+Phenobarb 250 mg.			
Time (min)	10	20	30	38
Av.Conc.(mg/ml.)	0.38	0.69	0.88	0.95
	PEG 4000,55%+PEG 1500,40%+Tween 60,5%+Phenobarb 250 mg.			
Time (min)	10	20	30	42.10
Av.Conc.(mg./ml.)	0.35	0.63	0.84	0.97
	PEG 4000,50%+PEG 1500,40%+Tween 60,10%+Phenobarb 250mg.			
Time (min)	10	20	30	42
Av.Conc.(mg/ml.)	0.35	0.62	0.82	0.94
	PEG 4000,45%+PEG 1500,40%+Tween 60,15%+Phenobarb 250mg.			
Time (min)	10	20	30	39.45
Av.Conc.(mg/ml.)	0.32	0.60	0.81	0.91
	PEG 4000,60%+PEG 1500,35%+Tween 60,5%+Phenobarb 250mg.			
Time (min)	10	20	30	41.35
Av.Conc. (mg/ml.)	0.32	0.60	0.81	0.91
	PEG 4000,60%+PEG 1500,30%+Tween 60,10%+Phenobarb 250 mg.			
Time (min)	10	20	30	42
Av.Conc.(mg/ml.)	0.33	0.63	0.82	0.93
	PEG 4000,60%+PEG 1500,25%+Tween 60,15%+Phenobarb 250 mg.			
Time (min)	10	20	30	36.30
Av.Conc.(mg/ml.)	0.33	0.61	0.81	0.90

Table 8. Releasing time and Concentration of Phenobarbital from different Combinations of bases and Tween 80.

PEG 4000, 60 % + PEG 1500, 40 % + Phenobarb. 250 mg.				
Time (min)	10	20	30	38
Av.conc.(mg/ml)	0.38	0.69	0.88	0.95
PEG 4000, 55% + PEG 1500, 40% + Tween 80, 5% + Phenobarb 250 mg.				
Time (min)	10	20	30	43.45
Av.conc.(mg/ml)	0.35	0.62	0.81	0.93
PEG 4000, 50% + PEG 1500, 40% + Tween 80, 10% + Phenobarb 250 mg.				
Time (min)	10	20	30	35
Av.conc.(mg/ml)	0.40	0.71	0.91	0.96
PEG 4000, 45% + PEG 1500, 40% + Tween 80, 15% + Phenobarb 250 mg.				
Time (min)	10	20	30	42.30
Av. conc.(mg/ml)	0.33	0.58	0.81	0.93
PEG 4000, 60% + PEG 1500, 35% + Tween 80, 5% + Phenobarb 250 mg.				
Time (min)	10	20	30	44
Av.conc.(mg/ml)	0.33	0.58	0.79	0.93
PEG 4000, 60% + PEG 1500, 30% + Tween 80, 10% + Phenobarb 250 mg.				
Time (min)	10	20	30	38
Av.conc.(mg/ml)	0.39	0.68	0.87	0.96
PEG 4000, 60% + PEG 1500, 25% + Tween 80, 15% + Phenobarb 250 mg.				
Time (min)	10	20	30	38
Av. conc.(mg/ml)	0.39	0.70	0.87	0.91

Table 9. Releasing time and concentration of Phenobarbital from different Combinations of PEG bases and Myrj 52

	PEG 4000,60% + PEG 1500,40%+ Phenobarb 250 mg.			
Time (min)	10	20	30	38
Av.Conc.(mg/ml.)	0.38	0.69	0.88	0.95
	PEG 4000,59%+PEG 1500,40% Myrj 52,1 %+Phenobarb 250 mg.			
Time (min)	10	20	30	39.30
Av.Conc.(mg/ml)	0.32	0.62	0.82	0.91
	PEG 4000,58%+PEG 1500,40% Myrj 52,2%+Phenobarb 250 mg.			
Time (min)	10	20	30	37.45
Av.Conc(mg/ml)	0.37	0 64	0.83	0.90
	PEG 4000,55 %+PEG 15000,40%+Myrj 52,5%+Phenobarb 250mg.			
Time (min)	10	20	30	31.45
Av.Conc.(mg/ml.)	0.385	0.71	0.90	0.95
	PEG 4000,50% +PEG 1500,40%+Myrj 52,10%+Phenobarb 250mg.			
Time (min)	10	20	30	32.45
Av.Conc.(mg./ml.)	0.39	0.68	0.84	0.88
	PEG 4000,60%+PEG 1500,35%+Myrj52,5%+Phenobarb 250 mg.			
Time (min)	10	20	30	38.30
Av.Conc.(mg/ml)	0.38	0.67	0.86	0.95
	PEG 4000,60%+ PEG 1500,30%+Myrj 52,10%+Phenobarb 250 mg.			
Time (min)	10	20	30	35.15
Av.Conc.(mg/ml)	0.36	0.66	0.86	0.91
	PEG 4000,60% +PEG 1500,25% +Myrj 52,15%+Phenobarb 250mg.			
Time (min)	10	20	30	37.30
Av.Conc.(mg/ml)	0.36	0.64	0.82	0.88

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