Susp. agents / HC – suspension

HPMC, HEC

Acacia [from Acacia trees] ↓ use as
- 35% dispersin in water (mucilage)
- High viscosity at pH 5 & pH 9
- Susceptible to microbial decomp.

Tragaconth [obtained from sap of Astragalus plant] ↓
- use as 6% dispersion in H_2O (mucilage).

MC
- Neutral, stable to heat & light
- Avail in various viscos. grades
- sol^n in cold H_2O
- pH 5

CMC
- Anionic
- Heat unstab. ⇓ ↓ viscosity
- Added in boiling H_2O & Then cool until dissolve
- doesn't contain oxidases that catalyze decomp of organic chemicals.
- Adv. over acacia = less is needed (6%).

Emulsifying Agents

Acacia ↓
- low viscosity emulsion.
- -ve charge anionic
- dehydrate easily
- Stable at pH ≥ 2–10
- req. preservative
- INCOM. ē → pervuian balsam, Bis. salts, carbonates
- O/W

Tragan
- good viscosity than aca.
- -ve charge anionic
- difficult to dehydrate
- 1/10th of acacia amount is used.
- O/W

Agar (source: red algae) ↓
- use to ↑se viscosity
- anionic
- affect by heating ⇒ dehydr. ⇒ destruction of charge.
- microbial degrad.

MC
- Neutral
- ↑ viscosity
- use ē mineral oil & cod-liver oil ⇓ Form O/W
- use in 2%
- viscosity grades of 15–4000 (centipoise unit) ⇓ viscosity
- ∴ Aca & Trag speci use = internal admin.

CMC
- ↑se visco.
- -anionic
- -formbasic sol^n
- -Tolerate 40% Alcohol
- -precipite in presence of free acids.

Pectin: use in same propar as Tragan. ⇒
Seems to be emulsifier "quasi emulsifier"

Brand name of a Type of magnesium-alum-Silicate: produced from refining clays

Suspending cont.

veegum — CLAYS — bentonite (found in clay of volcanic regions (volcanic ash))

- silicates - that're anionic in aq. disp.
- strongly hydrated
- exhibit thixotropy (becom gel — on standing, fluid — on agitation)

veegum: more hydrated than bento.

Bentonite: official form is 5% magma. — susp. agents

Thus = ↑ visco at same conc.

Other Agents

⇒ Xanthan Gum: ① cosolvent comptab. ② stable ③ high visco. relative to conc.

⇓ use ↑se. in modern formulations due to

Origin: produced through fermentation of carbohydrate by bacterium (Xanthomonas campestris) ↑bac. attack susceptibility

- agar, gelatin, pectin, gela. starch = costly
- carbomer (carbopol), Kaolin

⇒ levigating AGENTS: water, glycerin, alcohol or propylene glycol, mineral oil (common)

Method of prep:-

① levigation of solid = paste form. → geometric mix → susp.

② susp. agent + API → as an aq. dispersion or powdered form

Emulsifying cont.

Gelatin: good emulsifier in conc. 0.5-1.0%

May Anionic or cationic dep on iso-electric point

Types → Type A (+) = prep from acid treated precursor, use in acidic media

→ Type-B (-) = vice versa

PH at which mol = 0 charg denoted by PI

(PH < PI +ve charge) (PH > PI -ve charge)

Synthetic E·A

↑ HLB = ↑ Hydrophilic chain

① Anionic

- Sulfuric acid derivati
  - (SLS) Na-lauryl sulph
  - Na-Lauryeth sulph (SLES)
  - Triton X-200
- Sulfonic acid deriv
  - dioctyl Na Sulfosuccinate
  - Na-acetyl sulph
- Soaps
  - For external use
  - Have high pH & sensitive to acid
  - use as surface active agent (surfactant)
  - 1% conc.
  - incomp & electrolyte & addition.
  - Resis to ACID & Electroly ADDIT
  - SOAPs

Soaps

- Alkali soap
  - Hyrophili
  - Form O/W
  - (e.g NaOH / KOH + fatty acid) → Normal soap
- Metallic soap
  - water insol.
  - W/O
  - (metals other than alkali metals e.g = Al, Zn, Ca)
- Monovalent soap
  - O/W
- Polyvalent Ammonium soap
  - W/O.

② Cationic

- example
- (1) Benzalkon.Cl
  - (antimicrobial preservative in eye drops)
- (2) Quat. Am. compound (N Het) → use only in anti-septic creams
- (3) cetyl trimethyl
- (4) cetrimide.

③ Non-ionic

use in cosmetic, lubricant, food packaging

- Al-stearate
- Zn "
- Ca "

Span ← solubility enhancers → Tweens

- Sorbitan ester is know as span
- Hydrophobic
- W/O
- Low HLB

- a.k.a polysorbates
- Hydrophilic
- O/W
- ↑ HLB.
- form complex ē phenolic comps
- use to solubilize testosterone

Other surfactants: Nonoxynol 10, octoxynol 9, Sorbitan monopalmitate

Inorganic: ① Milk of Magnesia $Mg(OH)_2$ ② Mg oxide ③ Bentonite ④ carbowax.

- Dextrin (carbohyd) = use in cod liver oil emuls.
- Lipids = • phospholipids (lecithin – egg yolk) • wool alcohol
  - sterol (cholesterol, oil soluble alcohol) - O/W

OINTMENT BASES-

Oleaginous	Absorption	Emulsion	Water-soluble
• anhydrous	• anhydrous	★-W/O:	• anhydr./ or contain water
• Insolu in H_2O	• water insol.	• insoluble	• soluble.
• can't absorb H_2O	• CAN ABSORB H_2O	• can absorb H_2O	• absorb H_2O to the point of solub
• NOT water washable.	• NOT water washable.	• NOT water washable	• water washable
		• Permit H_2O-solub medication to incorporate through	O/W:
		Prior soln. = uptake as internal phase	• insoluble in H_2O
			• can absorb H_2O
			• Water washable

drug release POOR

← Oleaginous bases. (obtain from wool of sheep: Ovis aries)

Petrolatum
- good for oil-insolu ingred.
- absorb < 5% H_2O under normal cond.
- Doesn't becom rancid
- wax can be incorp. to stiffen the base.
- petrolatum - white petro.
- yellow ointment, white oint(s)
- paraffin, Mineral oil
- olive oil.

★-Petroleum jelly = (Mineral oil + wax)

Synthetic Esters
- can be use as constituent of Oleaginous base.

(1) Glyceryl monostear.
(2) Isopropyl myristate
(3) Isopropy palmitate
(4) butyl stearate
(5) butyl palmitate
(6) ★- long-chain-alcohol
(1) cetyl Al-OH (2) stearyl-OH (3) PEG

lanolin
- use in topical & cosmet

(1) lanolin oil
(2) Hydrog-enated lanolin

W/O ← Absorption BASES [Bees wax also included]

Wool Fat (anhydr. lanolin)
- high % of [cholesterol(1) + ester(2) + Alcohol(3) that contain Fatty Acids]
- Absorb twice its wt. water
- Melt b/w 36 & 42°C.

Hydrophilic petrolatum
- White petro comb. ē 8% Beeswax(2) 3% stearyl(3) alcohol & 3% chols. level(4)
- Added to W/O emulsifier
- prep form = AQUAPHOR

than
Superior?

EMULSION BASES

Spermaceti = obtain from head of sperm whale (solid wax)

Hydrous wool fat (lanolin)
- W/O emulsion
- contain 25% water

Cold cream
- W/O
- [melted white wax + spermaceti + expressed almond oil] mix toge.
- + Add hot aq. soln. of Na-borate and stir

To make more stable = use of mineral oil rather than almond oil

better emollient = ē almond oil

- should be freshly prep.

Hydrophilic ointm.
- O/W emulsion
- use SLS
- absorb 30-50% w/w ē out losing consistency

Vanishing cream
- (i) O/W
- (ii) contain large % of
  - water (present moisture 10%)
  - humectant (glycerin, propylene glycol) → retard moisture loss.
  - Stearic Acid = form film when water evaporate

PHARMACO-STUDY YOUTUBE CHANNEL

OTHER:
Dermovan, hypoallergenic, greaseless, unibase (non-greasy emul. base = absorb 30% of its wt in water and has pH close to skin).

WATER-SOLUBLE BASES → good drug release
PEG: Most widely!

3350 > 4000 more hygroscopic

PEG OINTMENT
- (blend of two solubl PEGs)
- solubilize both water sol. & inso. drugs
- COMPATIBLE ē WIDE RANGE DRUGS
- Contains (40% PEG 3350 + 60% PEG 400)
  - To use stiffness = PEG 3350 → 60%
  - (Made By FUSION METHOD).
- only (≤5%) liq. can added ēout loss of viscosity
- If 6-25% of aq. soln is to incorporated 5g/out of 40g PEG 335 can replace ē equal amount of stearyl Alcohol.

P.G (Propylene glycol) OR PG-Ethanol
- Form gel ē (2%) HPC (clear)

*-This base is Popular Dermatology Base.

Suppository Bases

Theobroma cacao seed found in dark chocolate

(Natural)

- most widely use — **Cocoa Butter** (Theobroma oil)
  - ★ - remain solid upto 32°C , 34-35 = Thin bland oily liqu.
  - ★ - congealing , 28 or less.

Composition	use	Limitation
• Mixture of TG of SOP-acids.	★ - Good for Rectal.	(1) inable to absorb aq. soln
• Exhibit polymorphism (4 - crystal forms). expres any one dep. on fusion temp.	★ - less ideal for (vagin, urethral).	[Add. of Non-ionic surfac. ↓se this problem] But cause ↓ instabil, ↓ Rancidity
		(2) MP ↓ by certain drugs e.g chloral hydrate

(Synthetic)

Witepsol

- TG of saturated F.A chain b/w C_{12} - L_{18}
- Lauric acid is major compt

- All 12 bases are
  - ✓ colorless
  - ✓ almost odourless
- Drug-releasing property of Witepsol H15 = similar to cocoa butter
- unlike cocoa butter
  - ✓ Doesn't exhibit polymorph. when heated & cooled.

	Melting	Congealing
	32-33	29-32

Small interval

- ✓ Solidify rapidly in mould = lubrication not req.
- ✓ Expensive.
- ✓ very stable.

Wecobee

(derived from coconut oil).

- ✓ Action similar to witepsol.
- ✓ Incorpor. of Glyceral monostear & propylen glycol monostearate make bases = more emulsifiable.
- ✓ Not widely available.

POWDER:-

1) INERT-DILUENTS:- Mostly use for hygroscopic, or deliquescent subst or eutetic mixtures (mix. That melt at a lower temp than any of their ingredients) to separate physic. interacting agents & absorb liquid materials

1) light Mg-oxide (2) Mg-carbonate (3) Kaolin
4) Starch 5) Bentonite

Mg-carbonate, Starch, lactose also use the absorbability of powders by using surface area.

- These 5 & SiO_2 are use as adsorbent in TABLETS

Capsule:-

Hard gelatin:- (1) gelatin + (2) opacifying agent (Titanium dioxide) + (3) SO_2 sulphur dioxide (0.15%) (to prevent decomposition of capsule) + colorant (4).

(use passage of light / make opaque / ↓ transparency)

Fill material: drug + diluent (lactose) + wetting agent (SLS) (to use dissolution) + mg. stearate (2%) lubricant (to use flow of material in case of auto or semi automated

000 (largest) capacity 600mg — 5 (smallest) 30mg.

- usually hard gelatin contain 65 mg – 1g. fill.

Soft-gelatin

spherical, oblong, elliptical.

Preservative (methyl & propyl paraben, sorbic acid. (to prevent fungal growth)) + Gelatin shell + plasticizer (polyhydric alcohol (sorbitol) e.g. or glycerin) + color.

Examp: D — Demeclocycline HCl (Declomycin, Lederle)
D — Digoxin (Lanoxicap, GSK)
A — vit.
C — vit. chloral hydrate
E

granibinan - Hydroxy Prog. dysleri (generic).

Aerosols Propellants

Compressed gases / air (also displacement agents)

- 1 - Nitrogen
- 2 - CO_2
- 3 - Nitrous oxide (N_2O)

a.k.a laughing gas

Liquefiable gases

Saturated HC

(1) propane
(2) n-Butane
(3) Iso-butane

Hydrofluorocarbons (2008)

stable, safe, effective

(1) 1,1,1,2-Fluoro-ethane (Propellant 134-A)

(2) 1,1 difluoroethane (propellent 152-A)

-ve effect on ozone & global warming → Banned by Montreal Protocol - 1996

Chlorofluorocarbons (CFCs)

Propellant-11	Propellant-12	Propellant 114
Trichloro-fluoro-methane	Dichloro-difluoro-methane	Tetra-fluoro-dichloro-ethane
a.k.a Freon-11		

Dimethyl ether

Pressurized containers: Tin-plated steel, Al, glass, plastic

MATRIX TABLETS

COMPONENTS

- Insoluble plastic
  1. polyethylene (PE)
  2. PVA
  3. Polymethacrylate (PMA) aka acrylic, acrylic glass.
- Hydrophilic polymer
  1) MC
  2) HPMC
- Fatty compound
  1) waxes
  2) Glyceryl tristearate

Examp: Gradumet (Abbott): Folic acid, Vit C & B complex Tablet.
Dospan (diethylpropion HCl): ↓ appetite, use to treat obesity.

Drug + matrix material → compress → Now coat a layer of drug for immediate release action.

Delayed/ENTERIC-COATED Tab

AGENTS used to coat

① Fat ② Fatty Acid ③ Waxes ④ Shellac ⑤ cellulose acetate phthalate (H_2O insoluble)

SUGAR-COATED

Sugar & its substitute

- Glucose
- Isomalt
- lactose
- Sugar-alcohol (a.k.a polyols) ½–⅓ sweeter than normal sugar

Sugar-alcohol examp
- mannitol, xylitol
- sorbitol, iso-malt
- Lactitol
- Hydrogenated starch hydrolysates → (HSH)

use in sugar-free formulation
obtain from fruit

Polishing Agents

- Beeswax
- paraffin
- Carnauba wax

Film-Coated

Coating material/film former

Thin layer of water-soluble/insoluble polymers
e.g. HPMC (Hypromellose), Hydrophilic
EC (Ethocel) – H_2O soluble
Povidone PVP – water + Non-polar solvents
PEG – H_2O soluble
- MC, HEC – H_2O soluble

Volatile = harmful when evapo in environ
aq = solvent = Not harmful.

Coating soln.

(1) Film-former
(2) alloying subs.
(3) Plasticizer (Diethyl Phthalate, Glycerin)
(4) Surfactant
(5) Opacifier
(6) Sweetner, flavour, color, glidant & volatile or aq. soln

TABLET-EXCIPIENTS

Diluents
- filler - bulk
- cohesiveness ↑
- Permit DC (direct compression)
- ↑ flow

- Ca-phosphate dihydrate (Di-Tab) (di basic), Ca-carbonate
- Ca-sulphate dihydrate
- cellulose (Microcrystal) (Avicel)
- cellulose derivatives
- Dextrose
- Lactose (simple, anhydrous, spray dried)
- Mannitol.
- Starches (directly compressible)
- Starches (hydrolyzed)
- Sorbitol
- Sucrose (powder)
- sucrose based material

Binders
cohesiven ← Dry form ← BINDERS → wet/liq form = granulation improve

- Corn starch (10-20% aq. soln/ starch paste)
- glucose soln (25-50% soln)
- Natural gums (e.g acacia) (Tragaca)
- cellulose derivative (MC, CMC, MCC) E.C
- Compressed sugar (Nu-Tab)
- Gelatin
- povidone PVP
- Sorbitol
- starch (pre-gelatinized)
- Alginic acid

Disintegrant
(Critical for dissolu and bioavail)

- Corn starch
- potato starch. a.k.a. (Primogel) super-disintg
- Starch deriv (Na-starch glycolate)
- Clay (e.g veegum, bentonite)
- crosspovidone (cross-linked PVP)
- cellulose derivatives (Na-CMC a.k.a., croscarmellose Na)
  ∴ Non-irritating purgative
- cation exchage resin
- Alginates, Alginic acid

Lubricants (↓friction)
- PEG
- Stearic acid. mg-stear.
- S.A (salts & derivatives)
- Talc
- Mineral oil.
- waxes
- surfactants

Mg-stearate = anti-adherent

Glidant
↑ flow ↓ adhesions of granules/powder

- Corn starch
- Silica derivati (colloidal silica) Aerosil. fumed silica
- Talc (colloidal silica)

Colors
(Food, Drug & Cosmetic FD&C)

Flavors
- 0.5-0.7% ↑
- Spray dried or oils

Sweetners
(250-500 x Sweeter than Sugar): carcinogenic
- Dextrose
- Saccharine
- Aspartam (200 x sweeter than
- glycerin
- Mannitol
- Lactose. Swe
- Sorbitol
- sucrose (cap locking - crystallize

Co-surfactants

- Glycerol
- Sorbitol
- butanol
- They're usually amino derivatives [C4–C10]

Preservative

- Methyl paraben, propyl paraben
- Benzoic Acid
- Chloroform water
- phenoxy-ethanol
- Dowicil 200 [brand]
- chlorocresol
- Quaternium 15 [generic]

Sunscreen

- ZnO_2
- TiO_2 → Opacifier in capsule, coating in Tab.

Gelling Agents

- Alginic
- Carbomer
- carboxy MC
- MC

ORasolv tab = effervescent.

Type

Drugs	Preffered Method	Reason
1) Digoxin	wet-granulation	low dose – needs uniformity
2) Aspirin	Dry-granulation	Moisture-sensitive
3) Mannitol	Direct compression	already good flow & compress
4) Melfamin	Dry/wet	poor compressibility
5) paracetamol	wet	needs ↑ Flows & ↓ compressibility
6) Multivitamin	wet	Complex formula, ↓ many active
7) vit-C	Dry granul.	Heat-sensitive
8) $NaHCO_3$	D. compress	High-dose-stable-compressible.