
田舎
なばなば
蜂味噌
椎茸昆布
旨煮
山椒風味
食べ歩るき
500円
3,000円以上
全国無料配送
由布岳
ゆずティー
1,200円

The HLB System

hydrophilic-lipophilic balance value

"A numerical representative of the hydrophilic and lipophilic tendencies of the material"

- used most in the rational selection of combinations of **nonionic emulsifiers**

- stable **o/w emulsion** can be prepared by utilizing HLB method

HLB Value

- Depends on the ratio of hydrophilic and lipophilic portion
  - low HLB values → soluble/ disperse in oil
  - high HLB value → soluble/ disperse in water

- Determined by the chemical composition and degree of ionization or hydration of the emulsifier molecule

HLB = ? hydrophilic gr. + ? hydrophobic gr.+7

$CH_3-(CH_2)_{10}-CH_2-O-S-O_3^-Na^+$

$$HLB = 38.7 + 12(-0.475) + 7$$
$$= 40$$

Rational Between HLB range and Surfactant Application

HLB Range	Use
0-3	Antifoaming agents
4-6	w/o emulsifying agent
7-9	Wetting agent
8-18	o/w emulsifying agent
13-15	Detergents
10-18	Solubilizing agents

Required HLB

- For calculating the relative quantities of emulsifying agents necessary to produce the most physically stable emulsion (o/w)

	o/w	w/o
Beeswax	5	12
Cetyl alcohol	-	15
Mineral oil	4	12
Soft paraffin	4	12
Wool fat	8	10

Rx			HLB
Mineral oil	35%		12
Wool fat		1	10
Cetyl alcohol		1	15
Emulsifier system		5	
Water to		100	

Proportion of each:

Mineral oil	35/37 x 100	= 94.6%
Wool fat	1/37 x 100	= 2.7%
Cetyl alcohol	1/37 x 100	= 2.7%

Total required HLB number

Mineral oil	94.6/100 x 12	= 11.4
Wool fat	2.7/100 x 10	= 0.3
Cetyl alcohol	2.7/100 x 15	= <u>0.4</u>
Total required HLB		12.1

This formulation requires an emulsifying agent blend of HLB 12.1

sorbitan monooleate (4.3)

polyoxyethylene sorbitan monooleate (15)

$$A = \frac{100\,(x - \text{HLB of } B)}{(\text{HLB of } A - \text{HLB of } B)}$$

A = the % conc. of the hydrophilic

B = the % conc. of the hydrophobic (100-A)

x = required HLB

$$A = \frac{100\,(12.1-4.3)}{(15-4.3)} = 72.9$$

$$B = 100-72.9 = 27.1$$

Total % of emulsifying blend = 5, then the % of each:

Sorbitan monooleate = 5 x 27.1/100 = 1.36

Polyoxyethylene sorbitan monooleate = 5-1.36 = 3.64

Have to be Remebered

- Degree of stability is at the optimal HLB value
- In choosing am emusifier blend, the effect of chemical structure on the type of interfacial film must be taken into account

    - long, staurated HC gr. Providing max. cohesion between adjacent molecule → condensed film

    - both emulsifying agents are of the same hydrocarbon chain length

Disadvantage of HLB System

- The inability to take into account:
  - the effect of temperature
  - the presence of additives
  - the concentration of emulsifier

Phase Inversion Temperature (HLB Temperature)

Temperature at which the emulsifier has equal hydrophilic and hydrophobic tendencies

For example:

o/w emulsion $\xrightarrow{\text{heat}}$ w/o emulsion

(nonionic emulsifiers)

As PIT ↑ → emulsion stability ↑

- At HLB temperature:

  the surfactant phase (isotropic liq., slightly grayish) appears between the oil and water

- For o/w emulsion

  HLB temperature should be ~ 55?C

- For w/o emulsion

  HLB temperature should be ~ 0?C

Using HLB Temperature for the Selection of Emulsifier

o/w emulsion

Oil + Aqueous
(all components of formulation)

↓ + 4% emulsifiers

Left thermostated at 55 ?C

↓

If separating into 3 transparent layers

↓

Selected for emulsification and
Determination of stability

Emulsion Properties

- Appearance and feel
- Particle size
- pH
- Viscosity

Appearance and feel

- due to:
  - Viscosity
  - Pour characteristics
  - Gloss
  - Smoothness
  - Pearlescence
  - Texture
  - Opacity

Factors influence emulsion Properties, Stability and Type

- Physical and chemical properties of the oil and water phases
- Phase-volume ratio of oil and water phases
- Concentration of emulsifier
- Order of addition ingredients
- Temperature of emulsification
- Type of equipment
- Method and rate of cooling

Particle Size

- Effects on:
  - viscosity
  - appearance
  - stability
- Depends on:
  - type and quantity of emulsifier
  - the amount of work done
  - order of addition ingredient

Particle size (?m)	Appearance
>1	White
0.1-1	Blue-white
0.05-0.1	Opalescent, Semitransparent
<0.5	Transparent

pH

- Skin:

  pH 4-6
- Soap-type emulsion:

  pH 8 or more

  separate if pH is reduced below 8
- Nonionic emulsified products:

  pH 3-10
- Cationic emulsified products:

  pH 3-7

Viscosity

"a measure of a fluid's resistance to change in form due to internal fiction"

- Unit: poise

  "the tangential force necessary to maintain a velocity of 1 cm^{-1} sec between 2 planes each 1 cm^2 in area and 1 cm apart"

- Common unit for defining viscosity:

  centipoises (cP = 0.01 poise)

- o/w emulsion:

adding synthetic → increasing visc.
natural gums, clays
certain emulsifiers

- w/o emulsion:

adding polyvalent metal soaps → increasing visc.
high melting point waxes

- A decrease in viscosity with age reflects an increase of particle size and is indicative of poor shelf life

Emulsion Stability

Stable emulsion:

"a system in which the droplets retain their initial character and remain uniformly distributed throughout the continuous phase"

- Creaming and Sedimentation
- Flocculation
- Coalescence (Breaking, Cracking)

Creaming and Sedimentation

- Creaming:
  the upward movement of dispersed droplets
- Sedimentation:
  the downward movement of dispersed droplets
- Both bring the particle closer together and may facilitate the more serious problem

Velocity of creaming:

indicated by Stoke's law

$$V = \frac{2a^2 g(? - ?)}{9?}$$

a = the globule radius

? = density of disperse phase

? = density of continuous phase

? = viscosity of continuous phase

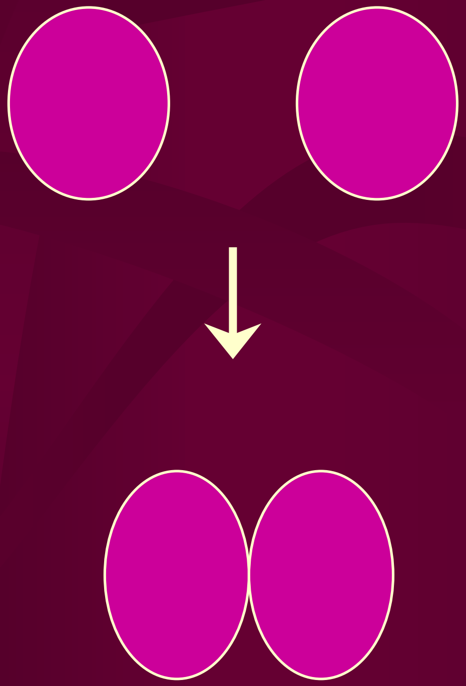
The rate of creaming will be decreased:

- By reduction in the globule size:
  - method
  - efficient emulsifier

2. By increasing in the viscosity of the continuous phase
3. By reduction in density difference between the 2 phases
4. By controlling of disperse phase concentration
   - <20%, creaming would occur readily
   - >60%, phase inversion occur

Flocculation

"Aggregation of the dispersed globules into loose clusters within the emulsion"



For simplest possible form (spherical), interparticle interaction and size distribution

$$\frac{dn}{dt} = -16?Da \,.\, n^2 = -\frac{8}{3}\,\frac{kT}{?}\,n^2$$

dn/dt = flocculation rate (P'cle/second.vol unit)

a = radius of droplet

D = diffusion coefficient for 1 droplet

n = number of p'cles per volume unit

k = Boltzmann constant

T = absolute temperature

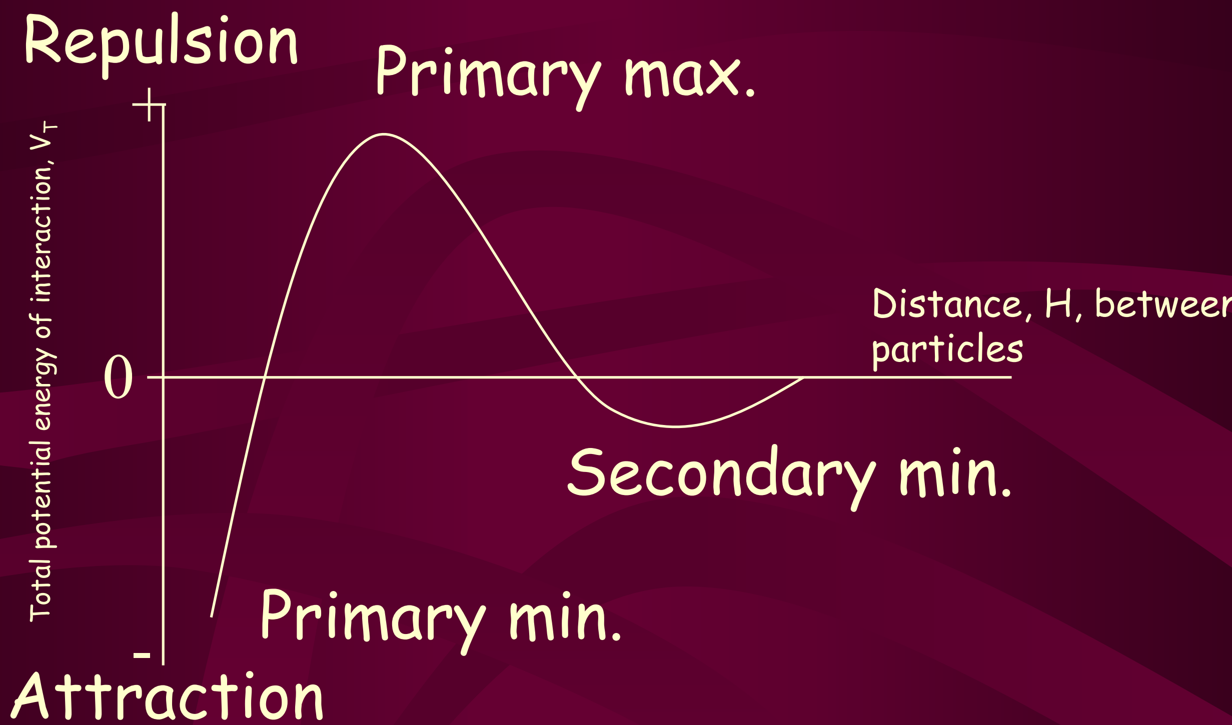
? = viscosity of continuous phase

$$t_{1/2} = \frac{3?}{8kTn}$$

If an energy barrier of height W (expressed in kT units, 4.1×10^{-21}J) is introduced between the particles

$$t_{1/2} = \frac{?\,(e^{W} + 2)}{8kTn}$$

- DLVO theory



$$V_T = V_A + V_R$$

V_A = van der Waals attraction

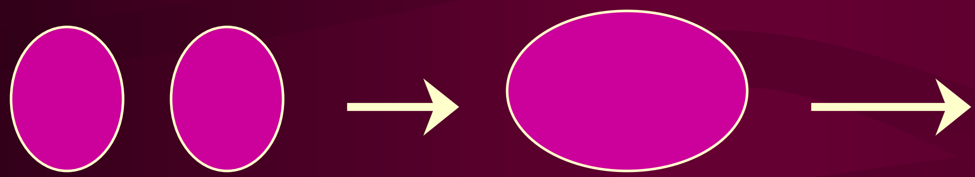
V_R = electrical repulsion

- Secondary minimum:

  Dispersion can be achieved by shaking

- High charge density on the dispersed droplets → high energy barrier → reduce the incidence of flocculation in primary emulsion

Coalescence



Cracking/Breaking

"Separation of an emulsion into its constituent phases"

Flocculation ⟶ Coalescence ⟶ separation

- Factors that cause an emulsion to crack:
- The addition of chemical that is incompatible with/insoluble the emulsifier
- Bacterial growth
- Temperature change

- Phase inversion may occur:

o/w (Na soap) + $CaCl_2$ ⟶ w/o (Ca soap)

Time for a droplet to move 5 cm in Vertical Direction[a]

[a]Density dufference = 200 kg m^{-3}

Viscosity = 0.01 P

r (?m)	time
100	11.5 sec
10	10 min
1	32 hr
0.1	133 days
0.01	36 years

Keeping the droplet size small is essential to delay an emulsion separation

Method of Assessing Stability

- Macroscopic examination

  - an examination of the degree of creaming or coalescence occurring over a period of time

  - calculating the ratio of volume of the creamed or separated part and the total volume and comparing these values
- Globule size analysis

  - microscopic examination

  - particle counting device (Coulter counter)

  - laser diffraction sizing
- Viscosity changes

Accelerated Stability Test

Employed for evaluating the stability of emulsions including:

- aging and temperature

  Cycling between 4?C and 45?C (on a 12 hr cycle for 10 cycles)

- Centrifugation

  at 3750 rpm in a 10 cm radius centrifuge for 5 hr = the effect of gravity for about 1 year

- Agitation

Stability Program

To assess the shelf life and quality control process

45 or 50?C   no separation for at least 60-90 days

37?C   no separation for at least5-6 months

RT   no separation for at least 12-18 months

4 ?C   no separation at least 1 month

- survive after 2/3 of freeze-thaw cycles (-20 and 25 ?C)

- survive after 6 or 8, at least, of heating/cooling cycles

between refrigerator temp. and 45 ?C (at each temp. of no less than 48 hr)

- no serious deterioration by centrifuging at 2000-3000 rpm at RT

- no adverse effect by agitation for 24-48 hr on a reciprocating shaker (~60 cycles per min. at RT and at 45 ?C)

Formulation of Emulsion

- Emulsifier selection (primary and auxiliary)
  - depends on dosage form
  - for auxiliary:
    natural gum and synthetic polymer →
    form excellent hydrophilic barriers
    (bentonite swell in water and strongly enhance the viscosity at pH>6)
    Carbomer
- Amount of emulsifier
- Selection of preservative, antioxidant, flavor, coloring agent

Absorption (Emulsifying) base

- anhydrous vehicles composed of a HC base and a substance that is miscible with HC but also carriers polar gr. (anhydrous lanolin and hydrophilic petrolatum)
- functions as a w/o emulsifier
- The water number = the max. amount of water that can be added to 100 g of such a base at a given temp.
- Hydrophilic ointment USP XIX

Example of oral emulsions

Mineral Oil Emulsion

Rx

Mineral oil	500	ml
Acacia (finely powdered)	125	g
Syrup	100	ml
Vanillin	40	mg
Alcohol	60	ml
purified water to	1000	ml

Use: a lubricating cathartic 30 ml, bed time

Preparation: Dry gum method

Have a good luck