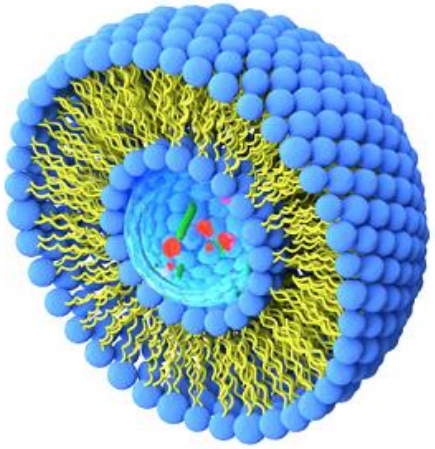
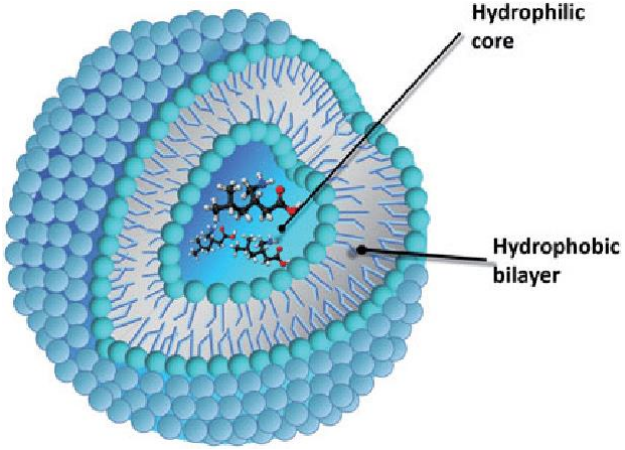


https://www.microfluidics-mpt.com/blog/webcast-training-on-creating-liposome-based-drug-delivery-systems



https://www.researchgate.net/figure/Liposome-for-drug-delivery_fig1_320661158

Targeted Drug Delivery System, LIPOSOME, Micro/nanoparticle, Colon DDS, Eritrosit DDS

Blok 8 Prodi Farmasi FKIK UMY

November 2023

UMY
UNIVERSITAS MUHAMMADIYAH YOGYAKARTA
Unggul & Islami

Outline

- 1. Targeted Drug Delivery System (DDS)
- 2. Liposome
- 3. Micro/Nanoparticle
- 4. Colon DDS
- 5. Erythrocyte DDS

Targeted Drug Delivery System

http://pubs.iscience.in/journal/index.php/cbl/article/view/941

Targeted Drug Delivery System

SELEKTIF dan hanya membidik target aksi

- It is a special form of drug delivery system where the pharmacologically active agent or medicament is selectively targeted or delivered only to its site of action or absorption and not to the non-target organs or tissues or cells.

- The drug may be delivered:
- To the capillary bed of the active sites.
- To the specific type of cell (or) even an intracellular region. Ex- tumor cells but not to normal cells.
- To a specific organ (or) tissues by complexing with the carrier that recognizes the target.

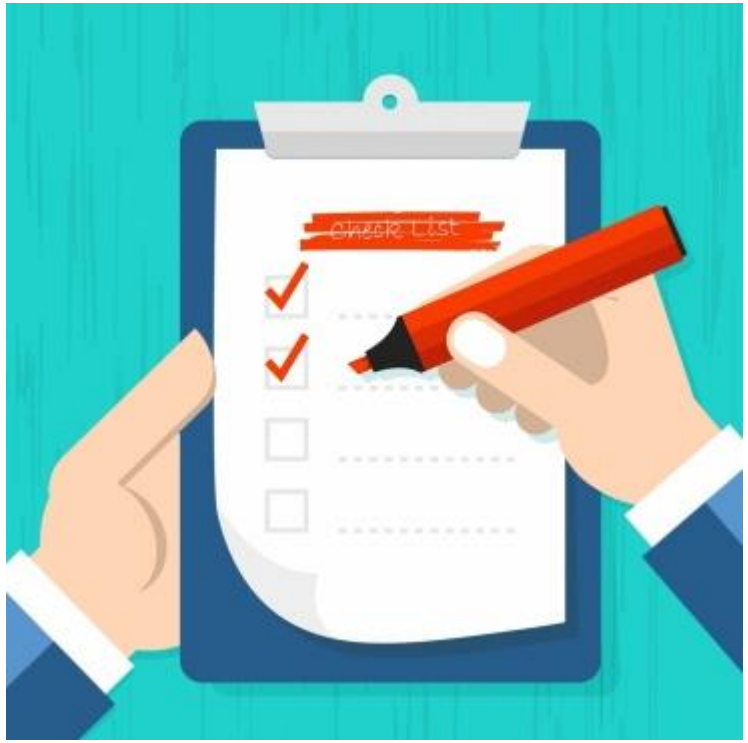
CONCEPT OF DRUG TARGETING

- Pertama kali disampaikan oleh Paul Ehrlich pada tahun 1902.
- Beliau merancang penghantaran obat sebagai “magic bullet” dan menggambarkan targeted drug delivery system adalah suatu kejadian dimana kompleks obat-pembawa menghantarkan obat secara eksklusif untuk target sel dalam cara yang spesifik (tertentu)
- “Targeted drug delivery implies for selective and effective localization of pharmacologically active moiety at preselected targets in therapeutic concentration, while restricting its access to non-target normal cellular linings, thus minimizing toxic effects and maximizing therapeutic index”.

Mengapa dibutuhkan system penghantaran obat yang tertarget?

Farmasetik	Farmakokinetik	Farmakodinamik
Ketidakstabilan obat pd konvensional	Absorpsi yang buruk	Spesifisitas yang rendah
Solubilitas yang rendah	Waktu paruh yang pendek	Indeks terapetik yang rendah
	Volume distribusi yang besar	

Karakter Ideal dari TDDS



- Biochemically inert (non-toxic)
- Non-immunogenic.
- Stabil secara fisika dan kimiawi, baik secara in vivo maupun in vitro
- Harus memiliki keseragaman distribusi kapiler
- Kecepatan pelepasan obat dapat dikontrol dan diprediksi
- Pelepasan obat tidak mempengaruhi aksi obat
- Jumlah obat yang dilepaskan yang dapat memberi efek terapetik
- Pembawa yang digunakan harus biodegradable atau sangat cepat dieliminasi dari tubuh tanpa kendala

Drug Targeting

Mengontrol distribusi obat dengan cara memasukkannya ke dalam suatu pembawa

Merubah struktur obat pada level molekular

Mengontrol obat ke dalam bio-environment untuk memastikan bio-distribusi yang terprogram dan diinginkan

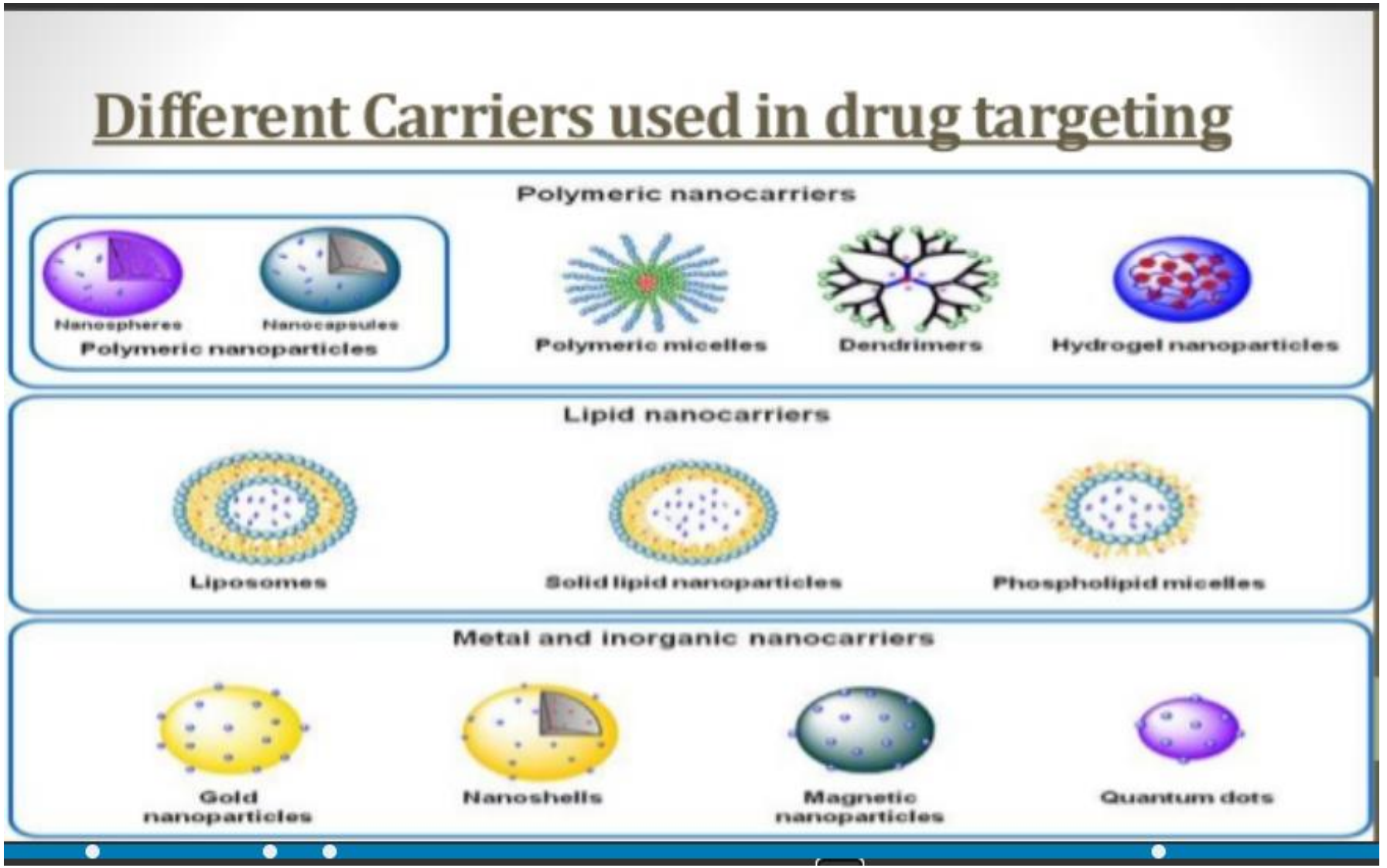
Component of Drug Targeting

TARGET:
Organ spesifik atau sel, atau kumpulan sel yang kondisinya secara kronik atau akut membutuhkan perawatan

PEMBAWA:
Molekul special atau system yang secara penting dibutuhkan untuk membawa muatan obat secara efektif kepada sisi yang ditarget

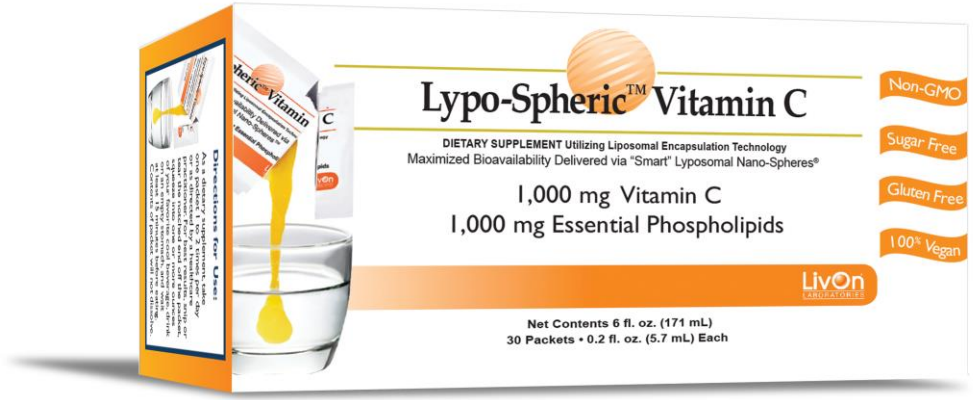
Kelebihan dan kekurangan

Kelebihan	Kekurangan
Toksisitas berkurang	Rapid clearance of targeted system
Obat cenderung tidak mengalami first pass metabolism	Terjadinya reaksi imun jika diberikan intravena
Berkurangnya dosis dan interval dosis	Deposisi obat pada target aksi dapat menimbulkan gejala toksisitas
Peningkatan absorbs dari molekul target	Sulit untuk menjaga kestabilan sediaan obat

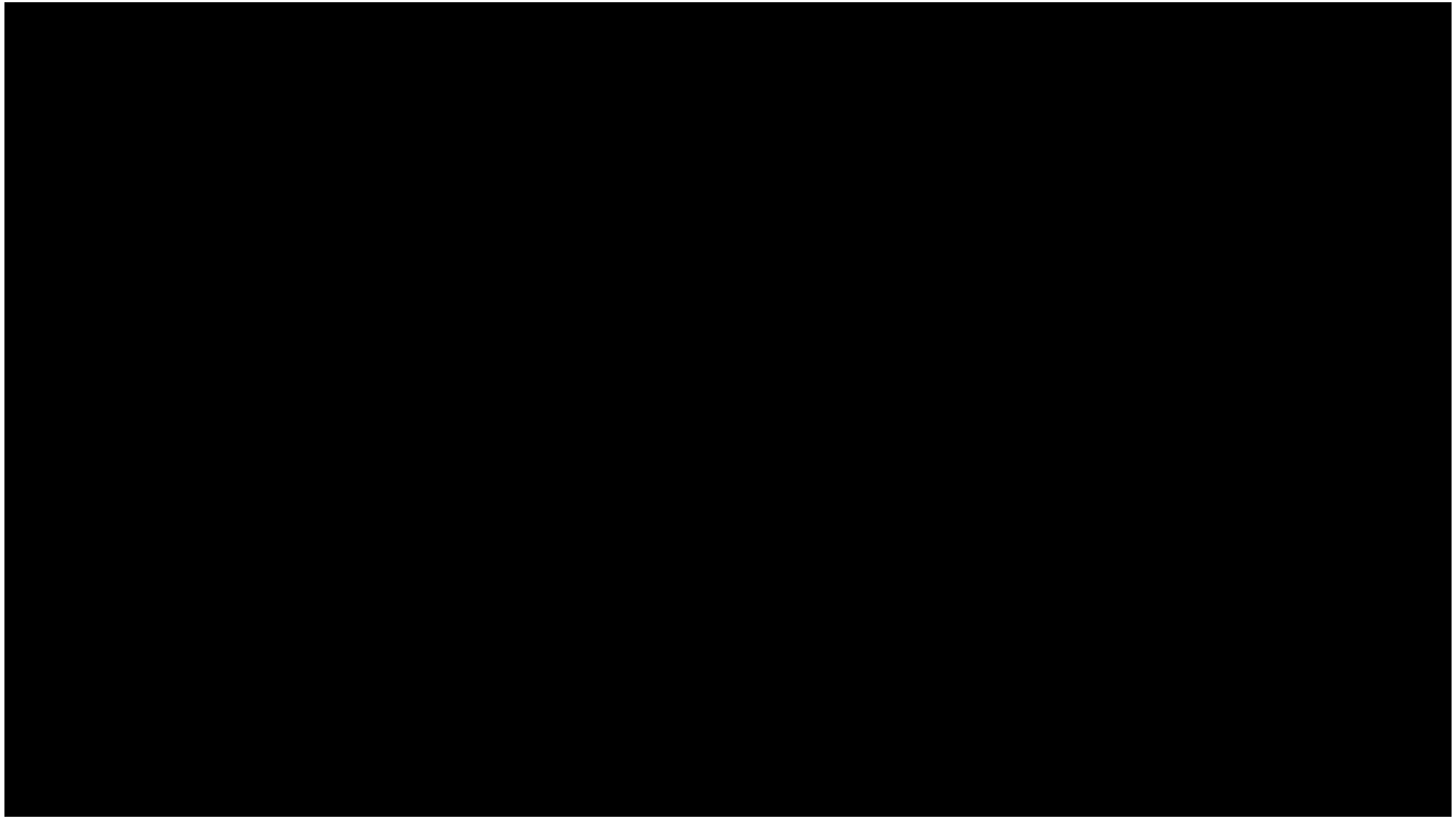

Different Carriers used in drug targeting
Polymeric nanocarriers
Nanospheres
Nanocapsules
Polymeric nanoparticles
Polymeric micelles
Dendrimers
Hydrogel nanoparticles
Lipid nanocarriers
Liposomes
Solid lipid nanoparticles
Phospholipid micelles
Metal and inorganic nanocarriers
Gold nanoparticles
Nanoshells
Magnetic nanoparticles
Quantum dots

Liposome

walmart.com



https://www.dougcookrd.com/vitamin-c-supplement/



https://www.youtube.com/watch?v=KQA9YlhgTQc&t=2s

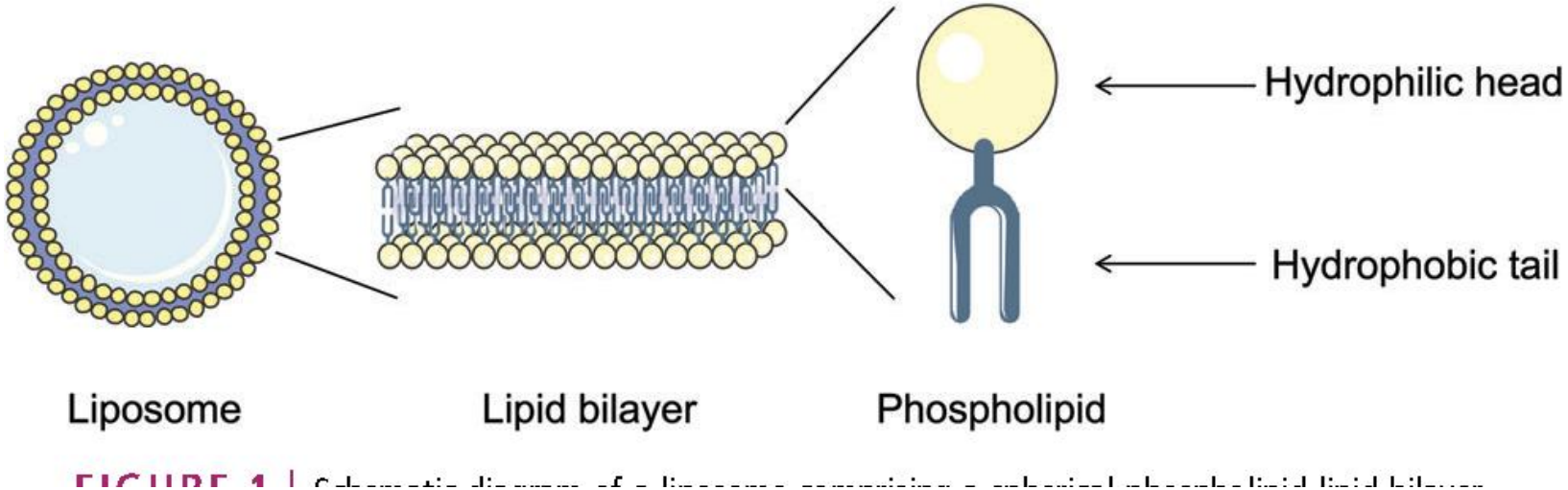
LIPOSOME

- Liposomes is Greek words means ‘Lipo’ mean ‘Fat’ and ‘Somes’ mean ‘Body’.
- Liposomes were first produced in England in 1961 by Alec D. Bangham.

LIPOSOME

Vesicle dengan bagian tengah adalah “suka air” ditutup oleh “lemak”

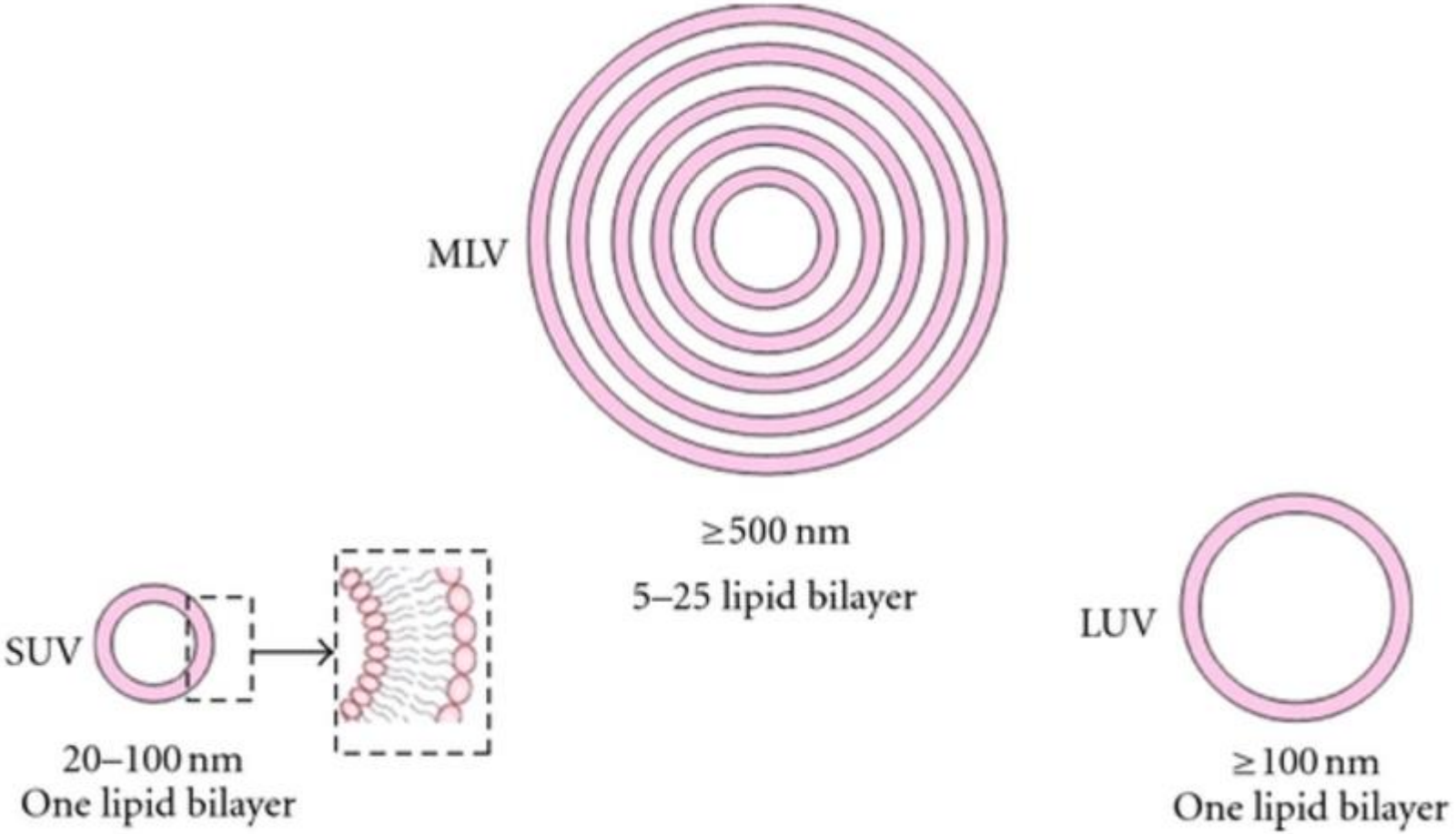
- Liposomes are simple microscopic vesicles in which an aqueous volume is entirely enclosed by a membrane composed of lipid molecule.
- Structurally, Liposomes are concentric bi layered vesicles in which an aqueous volume is entirely enclosed by a membranous lipid bilayers mainly composed of natural or synthetic phospholipids.
-



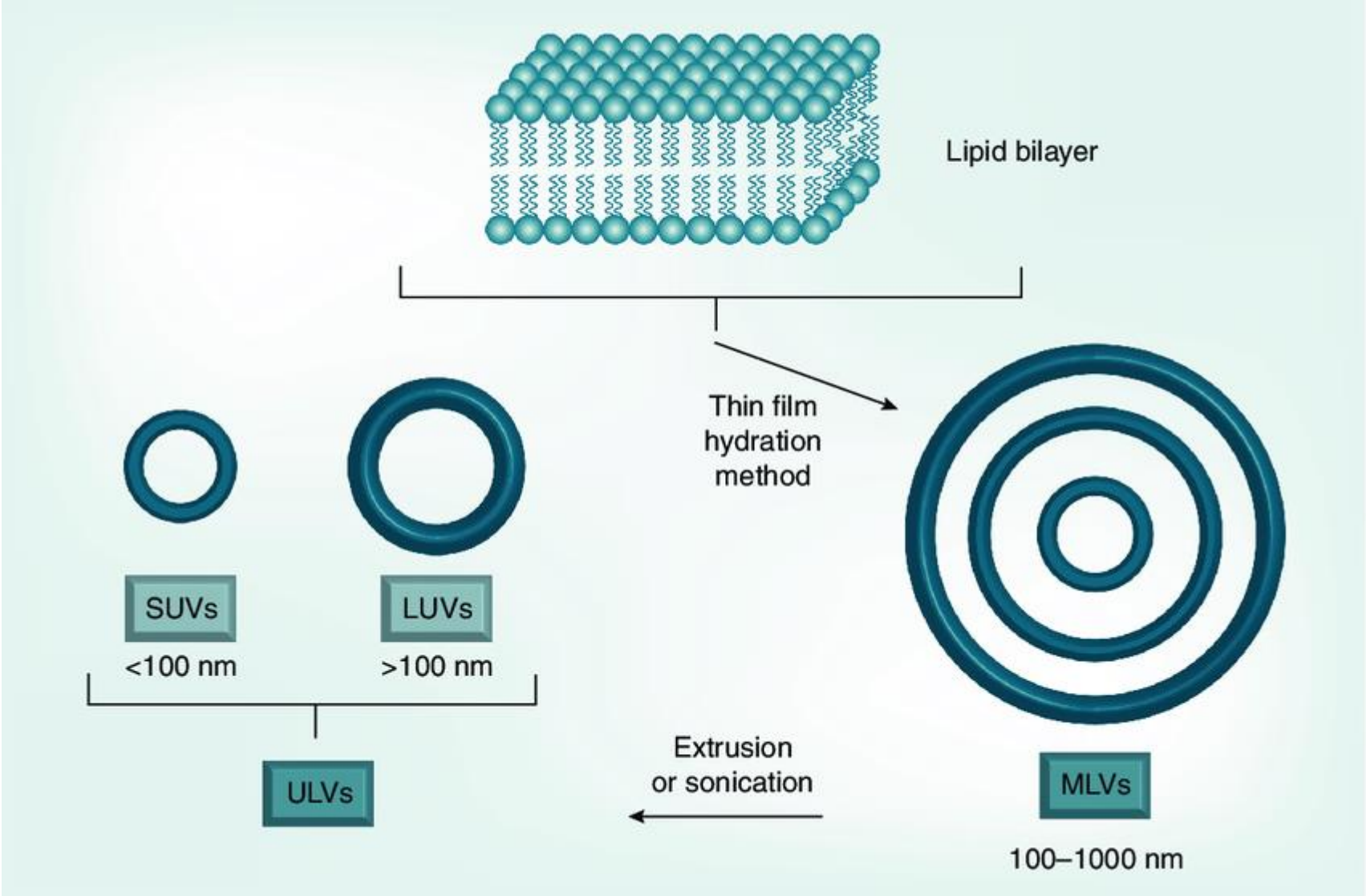
Semanticscholar.org

- Liposomes are vesicles in which an aqueous volume is entirely surrounded by a phospholipid membrane and their size can range between 30 and 50 nm up to several micrometers.
- They can consist of one (unilamellar) or more (multilamellar) homocentric bilayers of amphipathic lipids (mainly phospholipids). Based on their lamellarity (number of lamellae) — and size — they are characterized as SUVs/LUVs (small or large unilamellar vesicles) or MLVs (multilamellar vesicles).
- MLV liposomes are always large (at least cannot be considered small) and aqueous spaces exist in their center and also between their bilayers.

Classification of Liposome

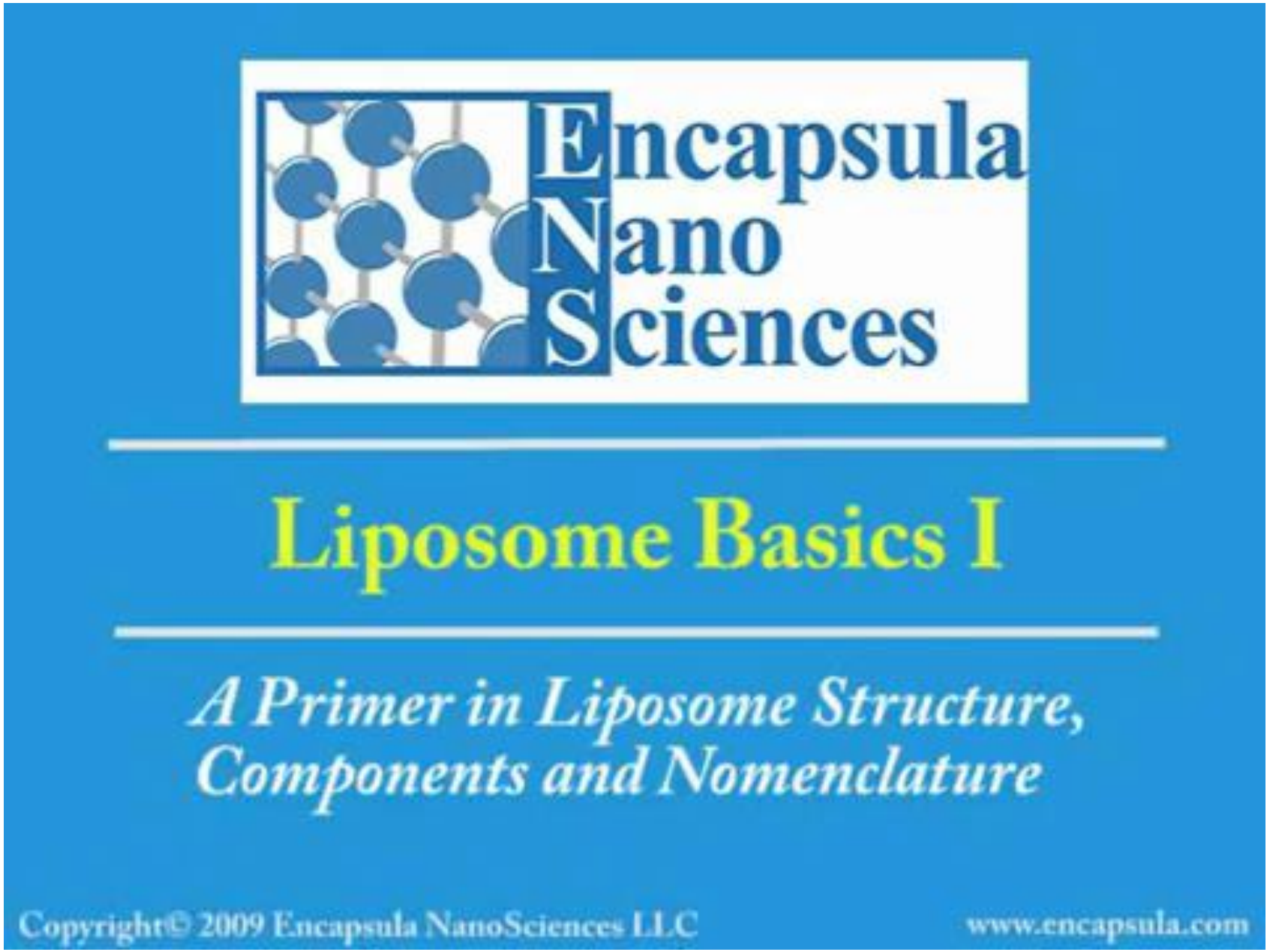


https://www.researchgate.net/figure/Classification-of-liposomes-and-their-relative-sizes-SUV-single-unilamellar-vesicles_fig3_234530457



https://www.researchgate.net/figure/Liposomes-of-different-size-and-number-of-lamellae-SUV-Small-unilamellar-vesicle-LUV_fig2_51744440

Liposomes of different size and number of lamellae. SUV: Small unilamellar vesicle; LUV: Large unilamellar vesicle; MLV: Multilamellar vesicle; ULV: Unilamellar vesicle.


Encapsula
Nano
Sciences
Liposome Basics I
A Primer in Liposome Structure,
Components and Nomenclature
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www.encapsula.com

COMPOSITION of LIPOSOMES

- Komponen Utama: Lecithin (mixture of phospholipids) dan cholesterol
- Fosfolipid: substansi lemak sebagai penyusun dinding sel dan membrane biologi

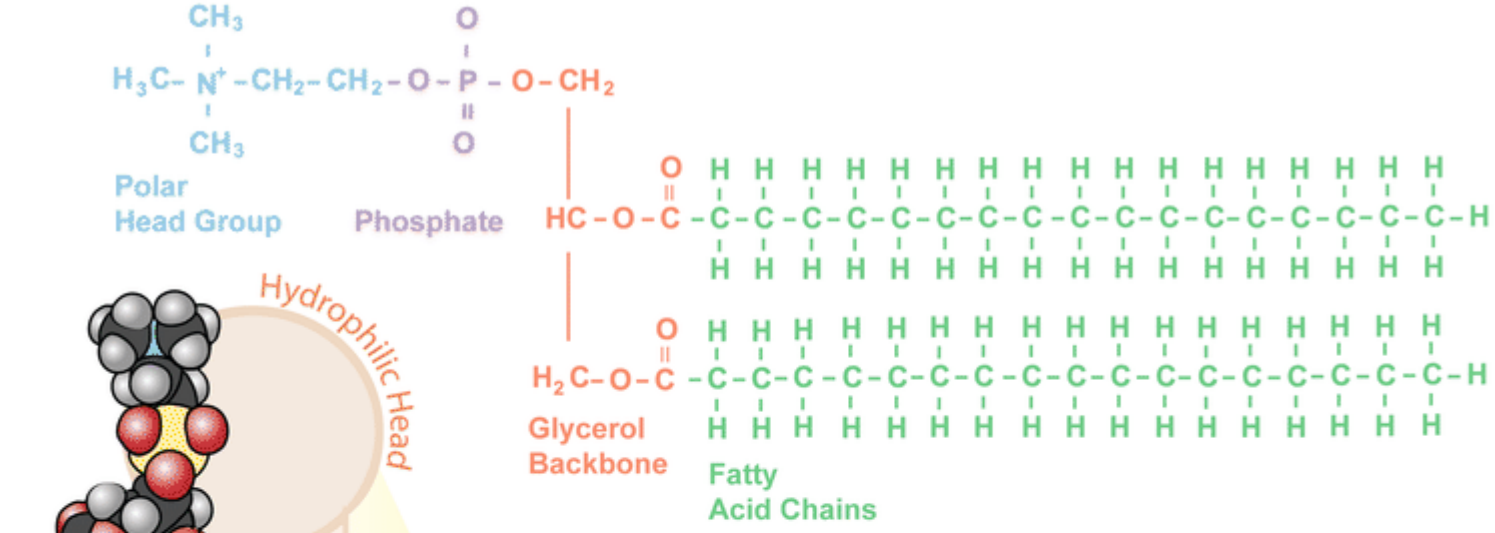
amphipathic moieties → with a hydrophilic head group and two hydrophobic tails.

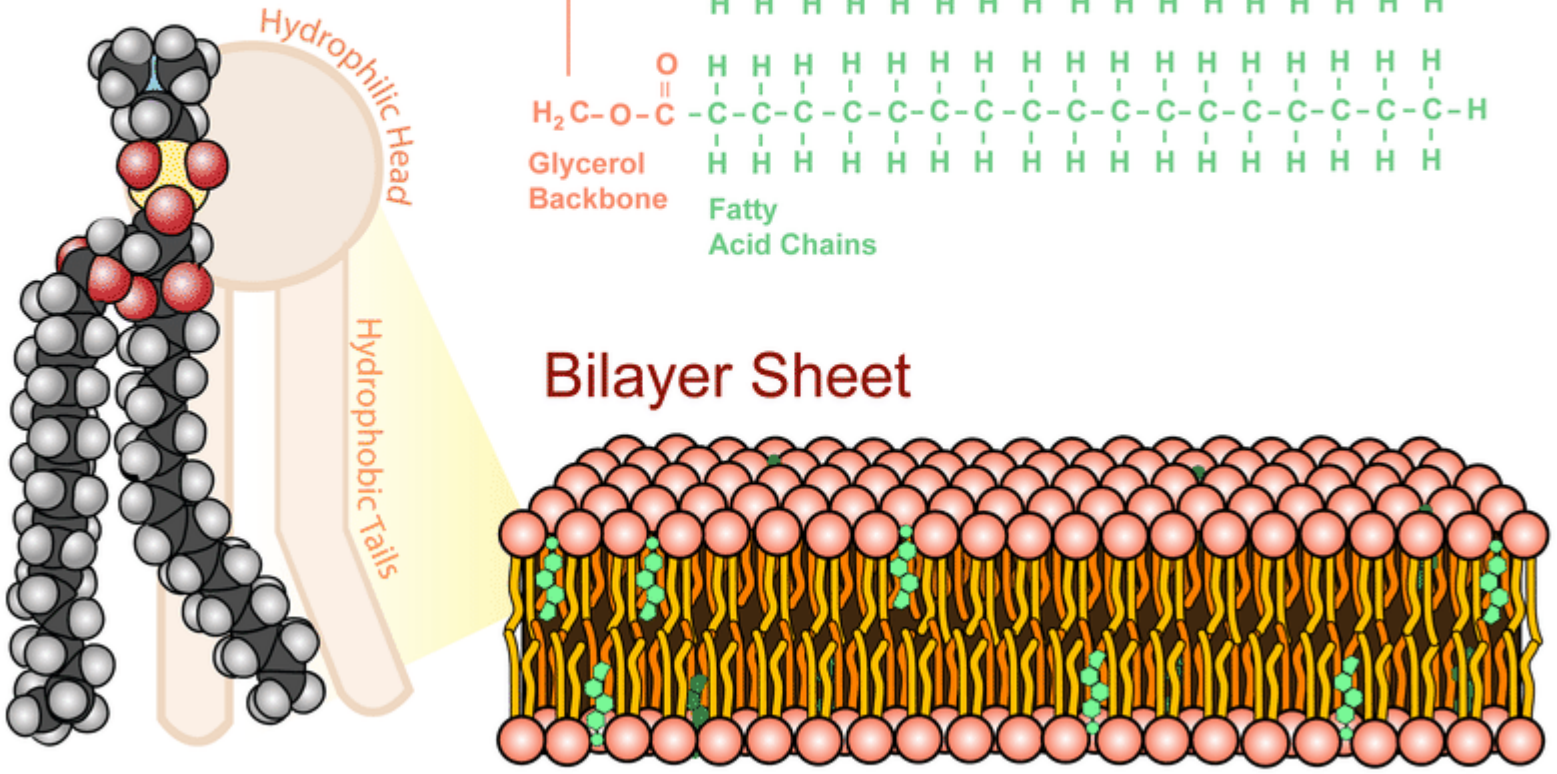
Fosfolipid memiliki bagian fosfatidil (ekor) dengan gugus kepala yang berbeda (choline, Etahnolamine, Serine)

Fosfolipid yang paling umum adalah fosfatidilkolin (phosphatidylcholine (PC) molecule)

Bi-layer lipid from PC

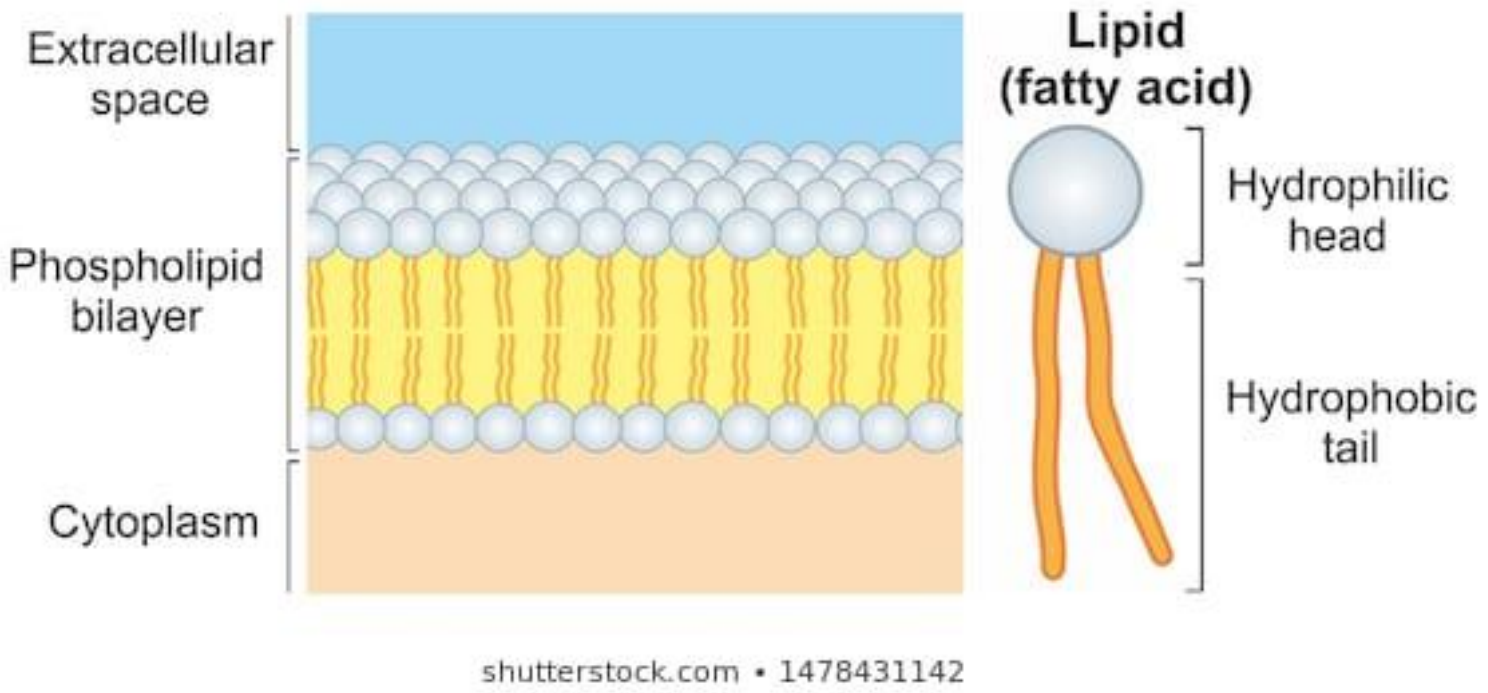
- Amphiphatic character
- Polar-head group region
- Non polar tail
- Phosphatidylcholine has glycerol bridge links a pair of hydrophobic acyl hydrocarbon chains having 10-24 carbon atoms with a hydrophilic polar head group.





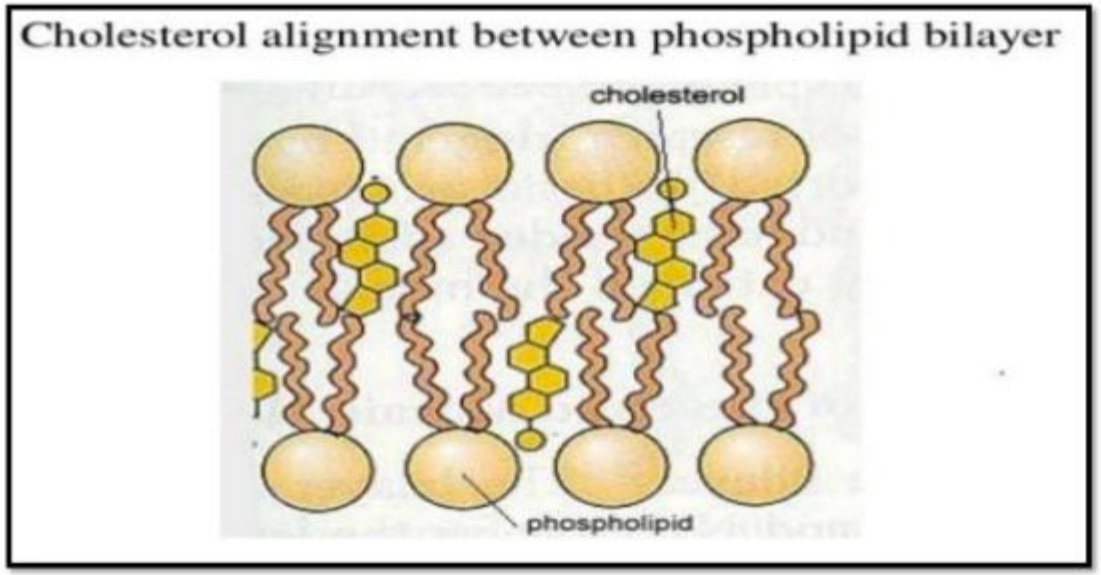
https://www.ck12.org/biology/phospholipid-bilayer/lesson/Phospholipid-Bilayers-BIO/?referrer=featured_content

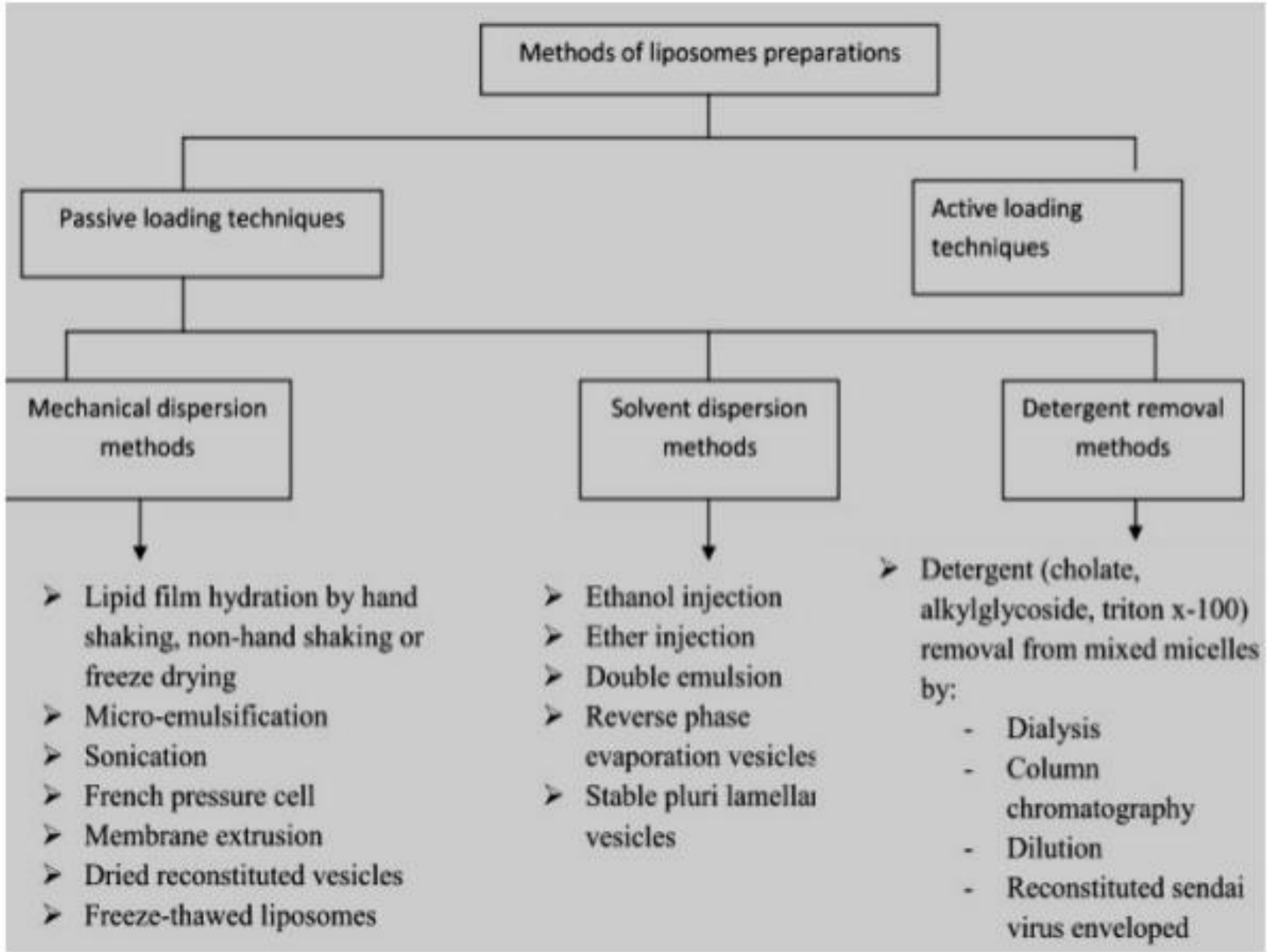
Phospholipid



Liposome Ingredient

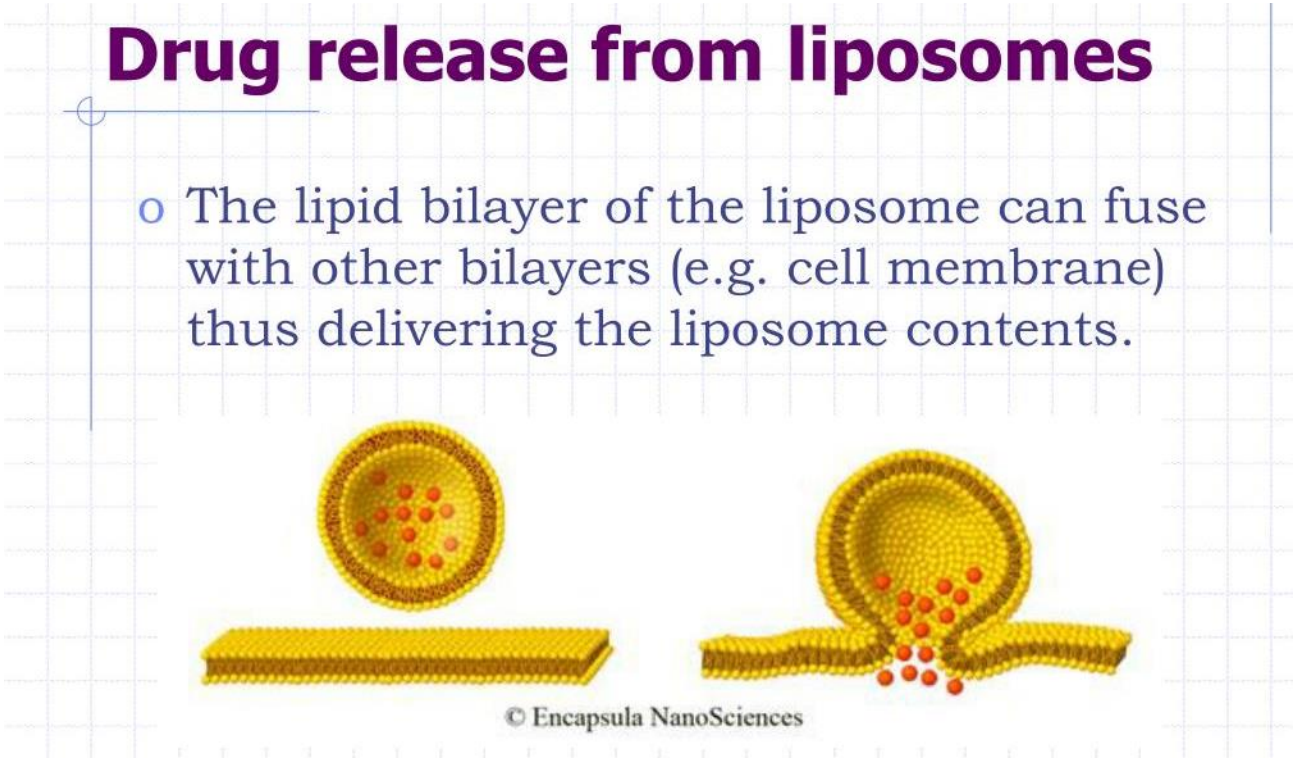
- Phospholipid Group (natural, semi sintetik, sintetik)
- Cholesterol → dapat ditambahkan ke bilayer tersebut untuk meningkatkan kekakuan




Methods of liposomes preparations
Passive loading techniques
Active loading techniques
Mechanical dispersion methods
Solvent dispersion methods
Detergent removal methods
Lipid film hydration by hand shaking, non-hand shaking or freeze drying
Micro-emulsification
Sonication
French pressure cell
Membrane extrusion
Dried reconstituted vesicles
Freeze-thawed liposomes
Ethanol injection
Ether injection
Double emulsion
Reverse phase evaporation vesicles
Stable pluri lamellar vesicles
Detergent (cholate, alkylglycoside, triton x-100) removal from mixed micelles by:
- Dialysis
- Column chromatography
- Dilution
- Reconstituted sendai virus enveloped

- Because the liposomes' outer shells imitate our cell membranes, liposomes can “fuse” with certain cells upon contact, delivering the liposome's content to the cell.

  This is the scientific advantage of the liposomal delivery system.



https://www.youtube.com/watch?v=7bPc6P7wRP4

Eur J Clin Nutr. Author manuscript; available in PMC 2019 Feb 25.
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Published online 2017 Aug 30. doi: 10.1038/ejcn.2017.132

PMCID: PMC6389332
NIHMSID: NIHMS1008081
PMID: 28853742

Oral supplementation with liposomal glutathione elevates body stores of glutathione and markers of immune function

Raghu Sinha,[1,*] Indu Sinha,[1] Ana Calcagnotto,[2] Neil Trushin,[2] Jeremy S. Haley,[3] Todd D. Schell,[3] and John P. Richie, Jr.[2,*]

Subjects/Methods

A 1-month pilot clinical study of oral liposomal GSH administration at two doses (500 and 1000 mg GSH per day) was conducted in healthy adults. GSH levels in whole blood, erythrocytes, plasma and peripheral blood mononuclear cells (PBMCs) were assessed in 12 subjects at baseline and after 1, 2 and 4 weeks of GSH administration.

Results

GSH levels were elevated after 1 week with maximum increases of 40% in whole blood, 25% in erythrocytes, 28% in plasma and 100% in PBMCs occurring after 2 weeks ($P<0.05$). GSH increases were accompanied by reductions in oxidative stress biomarkers including decreases of 35% in plasma 8-isoprostane and 20% in oxidized:reduced GSH ratios ($P<0.05$). Enhancements in immune function markers were observed with liposomal GSH administration including NK cell cytotoxicity, which was elevated by up to 400% by 2 weeks ($P<0.05$), and lymphocyte proliferation, which was elevated up to 60% after 2 weeks ($P<0.05$). Overall, there were no differences observed between dose groups, but statistical power was limited due to the small sample size in this study.

Conclusions

Collectively, these preliminary findings support the effectiveness of daily liposomal GSH administration at elevating stores of GSH and impacting immune function and levels of oxidative stress.

Keywords: glutathione, liposomal glutathione, supplementation, antioxidant, immune function

Liposome application

Dovepress
open access to scientific and medical research
International Journal of Nanomedicine

Int J Nanomedicine. 2017; 12: 6027–6044.
Published online 2017 Aug 21. doi: 10.2147/IJN.S132434
PMCID: PMC5573051
PMID: 28860764

Liposomal curcumin and its application in cancer

Ting Feng,[#1,*] Yumeng Wei,[#1,*] Robert J Lee,[2] and Ling Zhao[1]

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Abstract

Go to:

Curcumin (CUR) is a yellow polyphenolic compound derived from the plant turmeric. It is widely used to treat many types of diseases, including cancers such as those of lung, cervices, prostate, breast, bone and liver. However, its effectiveness has been limited due to poor aqueous solubility, low bioavailability and rapid metabolism and systemic elimination. To solve these problems, researchers have tried to explore novel drug delivery systems such as liposomes, solid dispersion, microemulsion, micelles, nanogels and dendrimers. Among these, liposomes have been the most extensively studied. Liposomal CUR formulation has greater growth inhibitory and pro-apoptotic effects on cancer cells. This review mainly focuses on the preparation of liposomes containing CUR and its use in cancer therapy.

Keywords: curcumin, liposomes, drug delivery, bioavailability, cancer

Liposomes as Drug Delivery Systems for the Treatment of TB

Marina Pinheiro; Marlene Lúcio; José LFC Lima; Salette Reis

DISCLOSURES | Nanomedicine. 2011;6(8):1413-1428.

1 Read Comment

Routes of Administration of Liposomes as Drug Delivery Systems for the Treatment of TB

Liposomes can be used as anti-TB nanocarriers for the treatment of both pulmonary and extrapulmonary TB; however, the success of therapy is highly dependent on the administration route of these nanoparticles.[64] Since liposomes are vulnerable to intestinal lipases, their administration needs to be performed by other routes different from the oral route.[65] The intravenous administration for TB treatment is compromised by several factors, such as leakage of liposome contents in the plasma compartment before reaching the target tissue, rapid clearance from the

Liposom dapat digunakan sebagai pembawa berukuran nano untuk penyakit TB paru

Micro/nano Particle

- **A nanoparticle is a small particle that ranges between 1 to 100 nanometres in size.**

Microparticles are particles between 1 and 1000 μm in size

Tujuan obat dibuat dalam nanoparticle

- untuk mengontrol ukuran partikel, sifat permukaan dan pelepasan zat aktif untuk memperoleh aksi spesifik obat secara farmakologis pada dosis regimennya

Keuntungan:

1. Memperbaiki sifat farmakokinetik dan farmakodinamik obat tanpa merubah struktur obat.
2. Meningkatkan efektivitas terhadap jaringan, penargetan jaringan, dan penargetan molekul.
3. Memiliki kemampuan untuk menghindari obat dari hambatan biologis.
4. Meningkatkan indeks terapetik obat.
5. Dapat pengirimkan beberapa obat yang sifat fisika kimianya berbeda.
6. Nanopartikel mengontrol dan melepaskan obat secara perlahan-lahan selama distribusi dan memodifikasi distribusi obat pada organ loka aksi,dan memperlambat klirens obat sehingga terapi obat dan meminimalkan efek samping

NANOPARTICLES TARGETED DRUG DELIVERY SYSTEM VIA EPIDERMAL GROWTH FACTOR RECEPTOR: A REVIEW

Vol 1, Issue 3, Sept - Dec 2019 Rusdin, Agus et al

- Overexpressing of epidermal growth factor receptor (EGFR) in specific organ implicates tumour aggression and proliferation. Therefore, EGFR becomes a primary consideration for targeted cancer therapy. Nanoparticle drug delivery system is a promising multifunctional technique to provide the targeted drug delivery system.

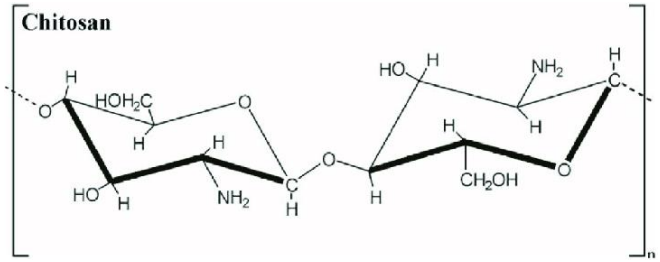
- EGFR-targeted drug delivery system could be a promising technique to provide high effectiveness of drugs in EGFR-positive cells cancers with lower side effects to non-tumour cells.

http://jurnal.unpad.ac.id/idjp/article/view/23613

TABLE 1 Classification of Natural and Synthetic Polymers and Their Methods of Purification or Synthesis

Polymer	Source	Method of Purification or Synthesis	Solubility
Sodium alginate	Natural (seaweed)	Alkali-based extraction	Water soluble (pH > 3), insoluble in organic solvents
Chitosan	Natural (crab shells)	Deacetylation of chitin	Soluble in aqueous solutions (low pH), insoluble in organic solvents
Gelatin	Natural (collagen)	Hydrolysis	Soluble in hot water (>34 °C), acetic acid, forms insoluble gel with water at room temperature, insoluble in organic solvents
Polysaccharides	Natural	Enzymatic reactions	Pullulans (soluble in water), dextrans (soluble in water)
Albumin	Natural (plants, animals)	Separation techniques (chromatography)	Soluble in water
Gliadin	Natural (wheat)	Alcohol extraction	Insoluble in water, soluble in ethanol
Poly(lactide) and Poly(lactide-*co*-glycolide)	Synthetic	Ring-opening polymerization	Insoluble in water, soluble in organic solvents
Poly(ε-caprolactone)	Synthetic	Anionic, cationic, free-radical, ring-opening polymerization	Soluble in select organic solvents such as chloroform, dichloromethane
Polyanhydrides	Synthetic	Melt condensation, ring-opening polymerization	Most polyanhydrides soluble in organic solvents, insoluble in water
Poly-alkylcyanoacrylates	Synthetic	Emulsion and interfacial polymerization	Soluble in organic solvents
Polyphosphoesters	Synthetic	Polyaddition, ring-opening	Available as water-soluble and water-

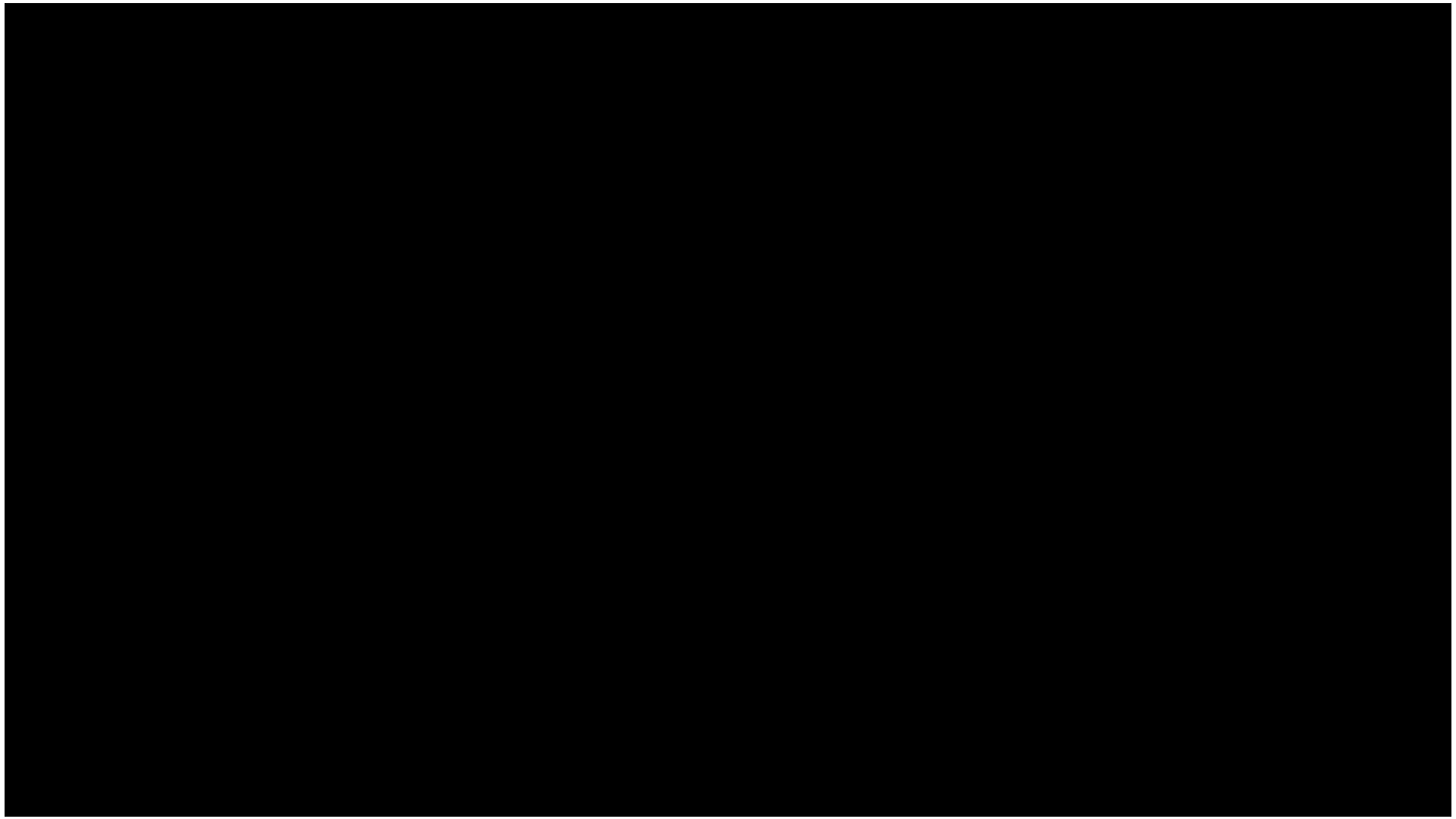
- Polimer alami:
  - Sodium alginate
  - Chitosan
  - Gelatin
  - Polisakarida
  - Albumin



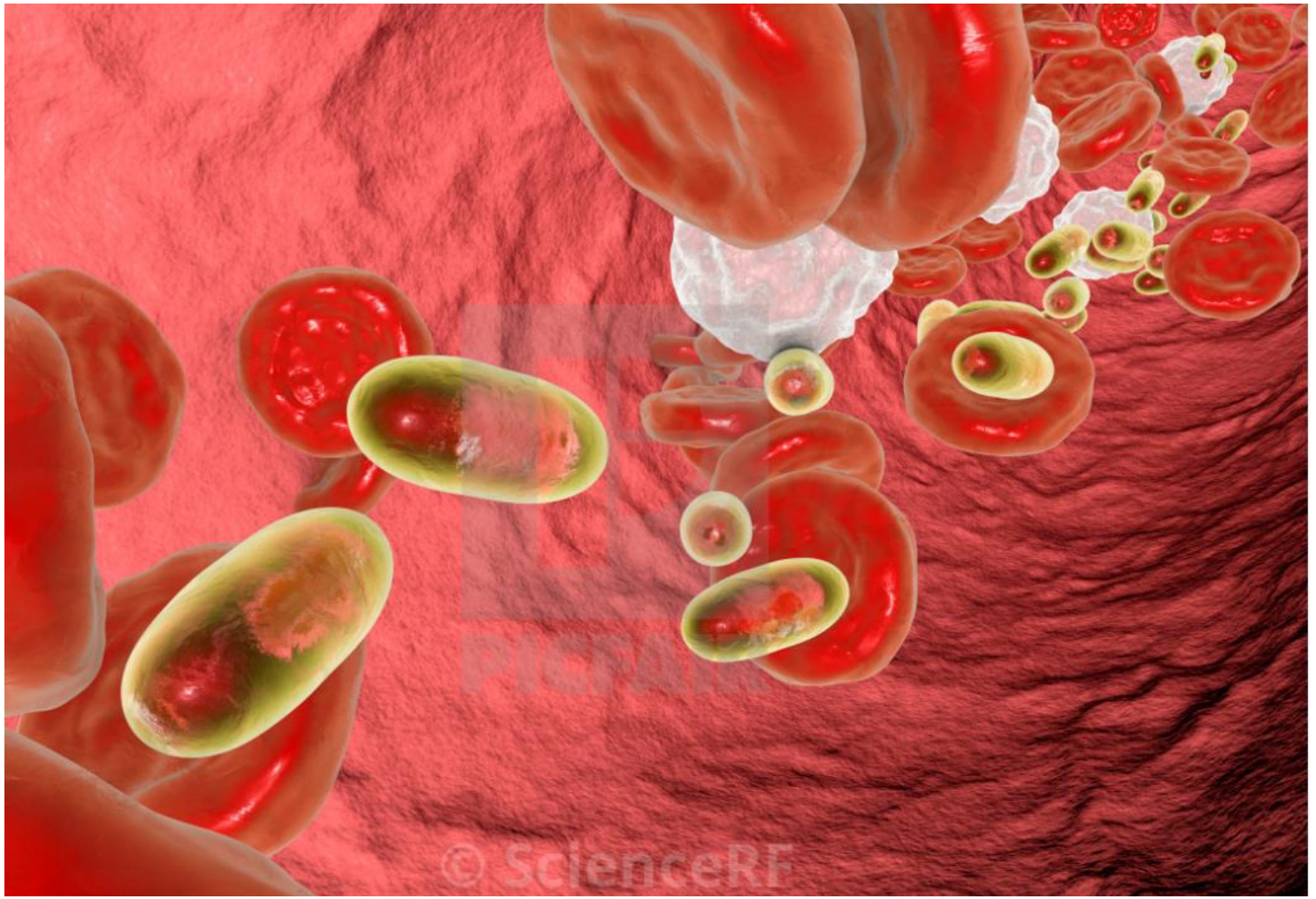
- Polimer Sintetik:
  - Gliadin
  - Polyphosphoester

Polimer: kitosan (chitosan)

- Polimer yang cukup popular digunakan dalam system nanopartikel adalah Kitosan.
- Kitosan memiliki beberapa sifat khas yaitu kemampuan membuka kaitan antarsel (tight junction) pada membrane usus sehingga sangat potensial untuk dikembangkan sebagai bahan pembuatan nanopartikel untuk aplikasi per oral.
- Biokompatibilitas kitosan dikarenakan kitosan merupakan polimer yang diperoleh dari hidrolisis polimer kitin yang berasal sumber alam yang sudah menjadi konsumsi umum pada cangkang hewan laut, sehingga cenderung tidak menimbulkan ketoksikan pada dosis terapi, selain dari sifatnya yang sekaligus biodegradabel



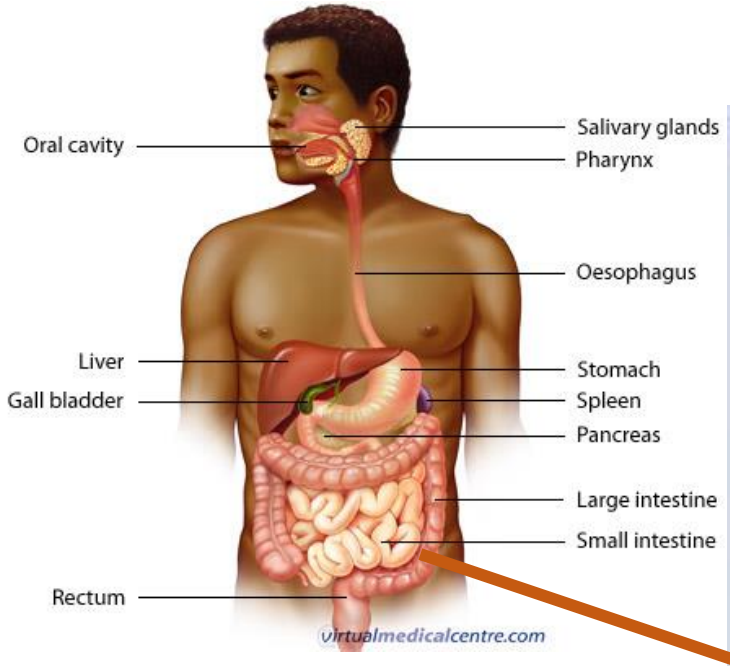
https://www.youtube.com/watch?v=RBjWwlnq3cA



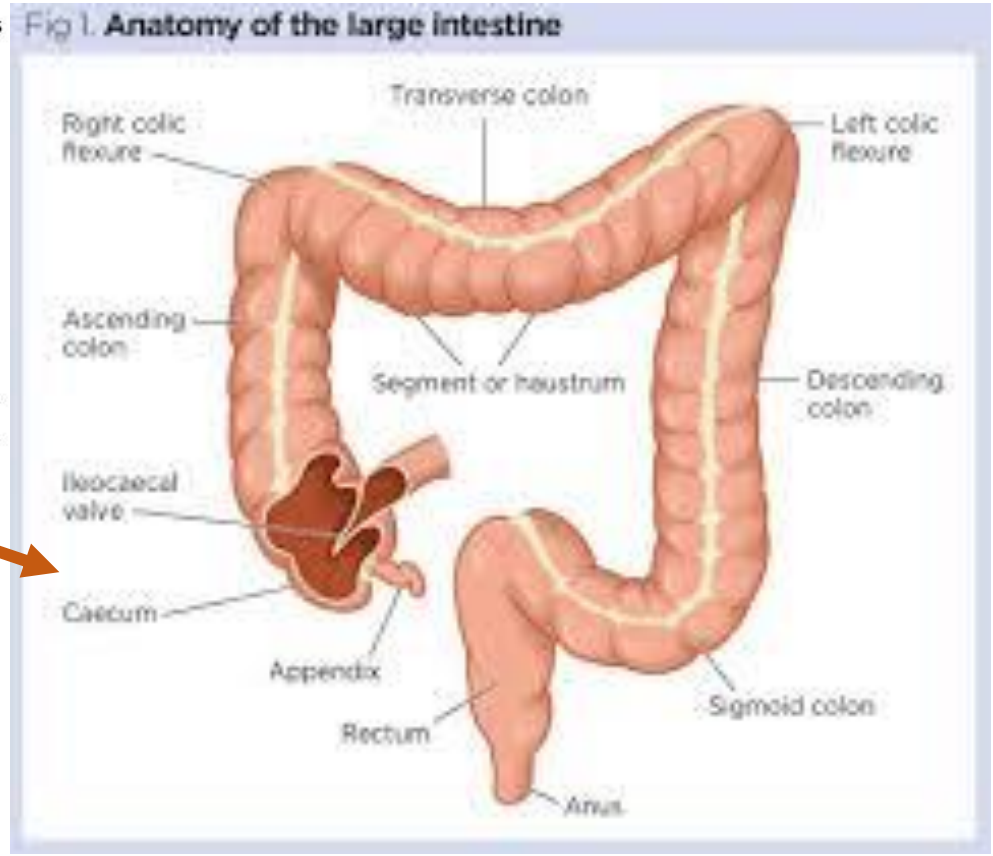
https://www.picfair.com/pics/05806456-chitosan-nanoparticles-in-blood-illustration

Colon Drug Delivery System

Anatomi Sistem Pencernaan



Healthengine.com.au



Nursingtimes.net

Usus besar atau kolon berbentuk tabung muskular berongga dengan panjang sekitar 1,5 m yang terbentang dari caecum (sekum) hingga kanalis ani. Diameter usus besar lebih besar sari usus halus,yaitu sekitar 6,5 cm, tetapi makin dekat anus diameternya semakin kecil.

Usus besar terdiri dari sekum, kolon dan rectum
Kolon (sekitar 1 m panjangnya) dibagi menjadi kolon ascenden, kolon transversum, desenden, dan sigmoid

Penyakit colon

- Ulceratif colitis
- Carcinoma
- Infeksi
- Chron’s disease : salah satu penyakit radang usus kronis yang menyebabkan peradangan pada lapisan dinding sistem pencernaan, mulai dari mulut hingga anus. Namun, kondisi ini lebih sering ditemui terjadi pada bagian usus halus dan usus besar (kolon)

CDDS

- Colon targeted drug delivery system (CDDS) merupakan metode pengobatan penyakit yang ditujukan atau disampaikan langsung ke lokal usus.
- Harus dapat melindungi obat dari rute hingga kolon
- Pelepasan obat dan absorpsi obat tidak boleh terjadi di lambung/usus halus.
- dissolusi dan degradasi bioaktif terjadi di kolon
- Kolon merupakan tempat yang tepat dalam absorpsi obat, peptide, protein karena

1. Cenderung tidak dipengaruhi enzim pencernaan dan keragaman dalam pencernaan
2. Aktivitas proteolitik pada mukosa kolon sangat kecil daripada di usus halus, sehingga CDDS melindungi obat peptide dari hidrolisis dan degradasi enzimatik di duodenum dan jejunum. Obat dilepaskan di ileum atau colon sehingga terjadi bioavailabilitas sistemik yang besar.
3. Waktu tinggal (residence time) di kolon cukup lama bisa samapi 5 hari dan memiiki responsivitas yang tinggi terhadap percepatan absorpsi

CDDS

- Pada sistem penghantaran ini telah dibuat berbagai macam sediaan, salah satunya adalah tablet dengan variasi penyalutan yang berbeda-beda seperti kombinasi polisakarida, polimer dan lain-lain.
- **Secara konvensional, polisakarida digunakan dalam formulasi tablet untuk menghambat pelepasan obat**
- Polisakarida digunakan sebagai matriks atau sebagai bahan penyalut. Pada matriks, diperlukan konsentrasi polimer yang tinggi atau dapat digunakan sebagai pengikat dalam tablet. Dengan demikian, berbagai polisakarida dan konsentrasinya mempengaruhi pelepasan obat dari tablet.
- **Dalam formulasi sediaan ini yang berperan dalam penentuan farmakokinetika dan distribusi selular obat adalah perilaku molekul karier (pembawa) sediaan**
- Adapun beberapa polisakarida yang digunakan seperti kombinasi kitosan (chi) dan kondroitin sulfat (CHS) (Gattani,2009), pektin (A. Akhgari dkk, 2010), dan inulin (A. Akhari, 2009)

Table 1

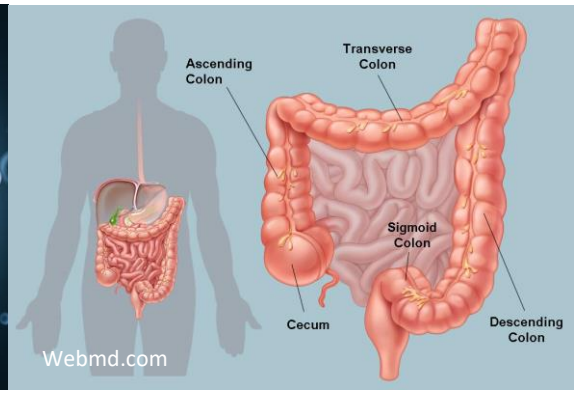
Colon targeting diseases, drugs and sites

Target sites	Disease conditions	Drug and active agents
Topical action	Inflammatory Bowel Diseases, Irritable bowel disease and Crohn's disease. Chronic pancreatitis	Hydrocortisone, Budenoside, Prednisolone, Sulfaselazine, Olsalazine, Mesalazine, Balsalazide.
Local action	Pancreatactomy and cystic fibrosis, Colorectal cancer	Digestive enzyme supplements 5-Flourouracil.
Systemic action	To prevent gastric irritation To prevent first pass metabolism of orally ingested drugs Oral delivery of peptides Oral delivery of vaccines	NSAIDS Steroids Insulin Typhoid

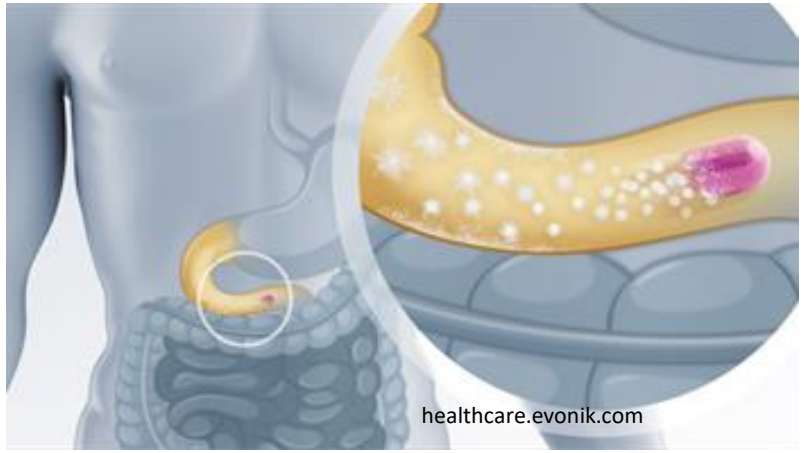
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3215502/

Tujuan CDDS

- Meningkatkan penggunaan obat
- Menurunkan efek samping
- Menurunkan dosis yang dibutuhkan
- Obat secara langsung tersedia di target aksi di kolon → meningkatkan efek terapetik
- Penggunaan secara oral efektif dalam mengatasi penyakit kolon



Pendekatan CDDS



- 1. Ph dependent
- 2. time dependent memperpanjang waktu lag 5-6 jam
- 3. microbially triggered system jumlah bakter di colon 1011-1012 CFU/mL

    400 species

    Predominant species: Bacteroides, bifidobacterial, eudobacteria, enterococcus, enterobacteria

    Mayoritas proses metabolic di kolon : hidrolisis dan reduksi
- 4. Kombinas 1 dan 2

pH dependent delivery

- Dilapisi dengan polymer yang ph sensitive
- Melarutnya polymer dipengaruhi oleh pH
- Pelapisan dapat single layer atau multi layer
- GI residence time parameter
- Methacrylic acid copolimers – eudragit
- Obat tdk lepas dibawah pH 7

GI tract segment	pH
Stomach	1-3
Small intestine	5-7.5
Large Intestine	6.8-7.8
Rectum	7.8-8

Timed released system

- Menunda pelepasan obat hingga sampai ke kolon
- Melepaskan obat setelah mencapai predetermined lag time
- Lag time dimulai sejak pengosongan lambung karena kebanyakan formulasi dari time-controlled adalah enteric coated

- Pelepasan obat dg system ini tidak dipengaruhi pH

Oman Med J

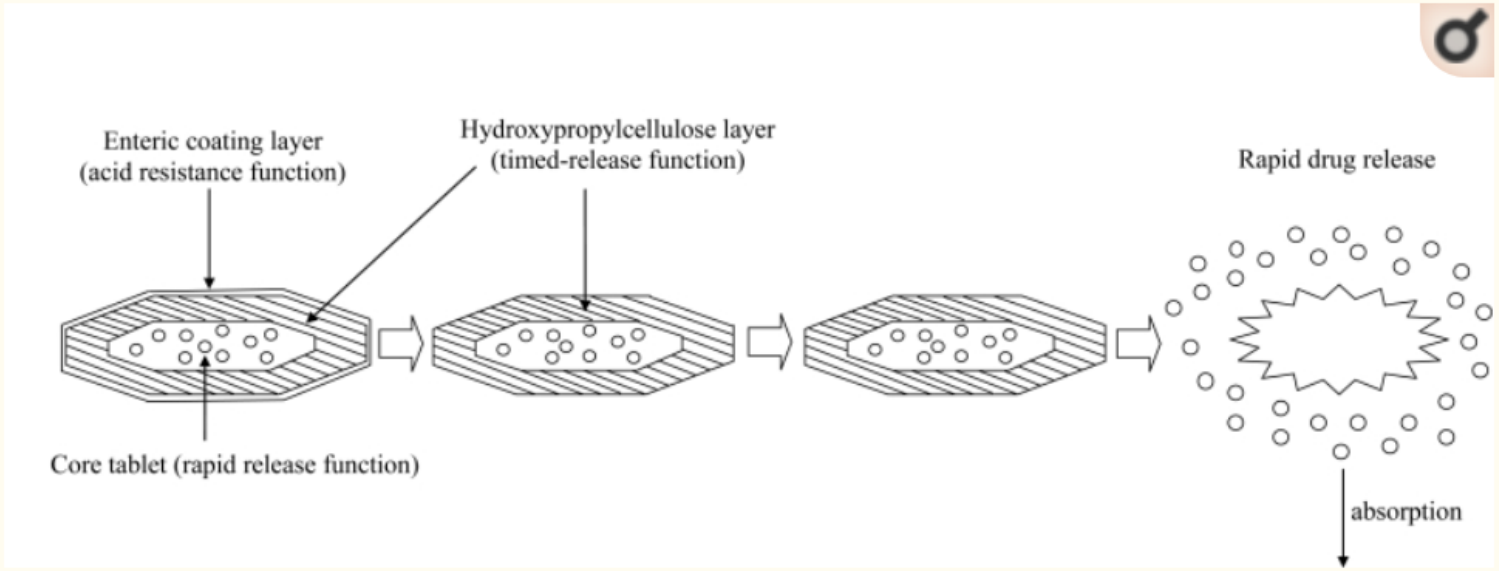


Figure 1

Design of enteric coated timed-release press coated tablet (ETP Tablet)

- Polisakarida alami sebagai polimer dalam colon dds chitosan, guar gum, almond gum, pectin, dextran, inulin

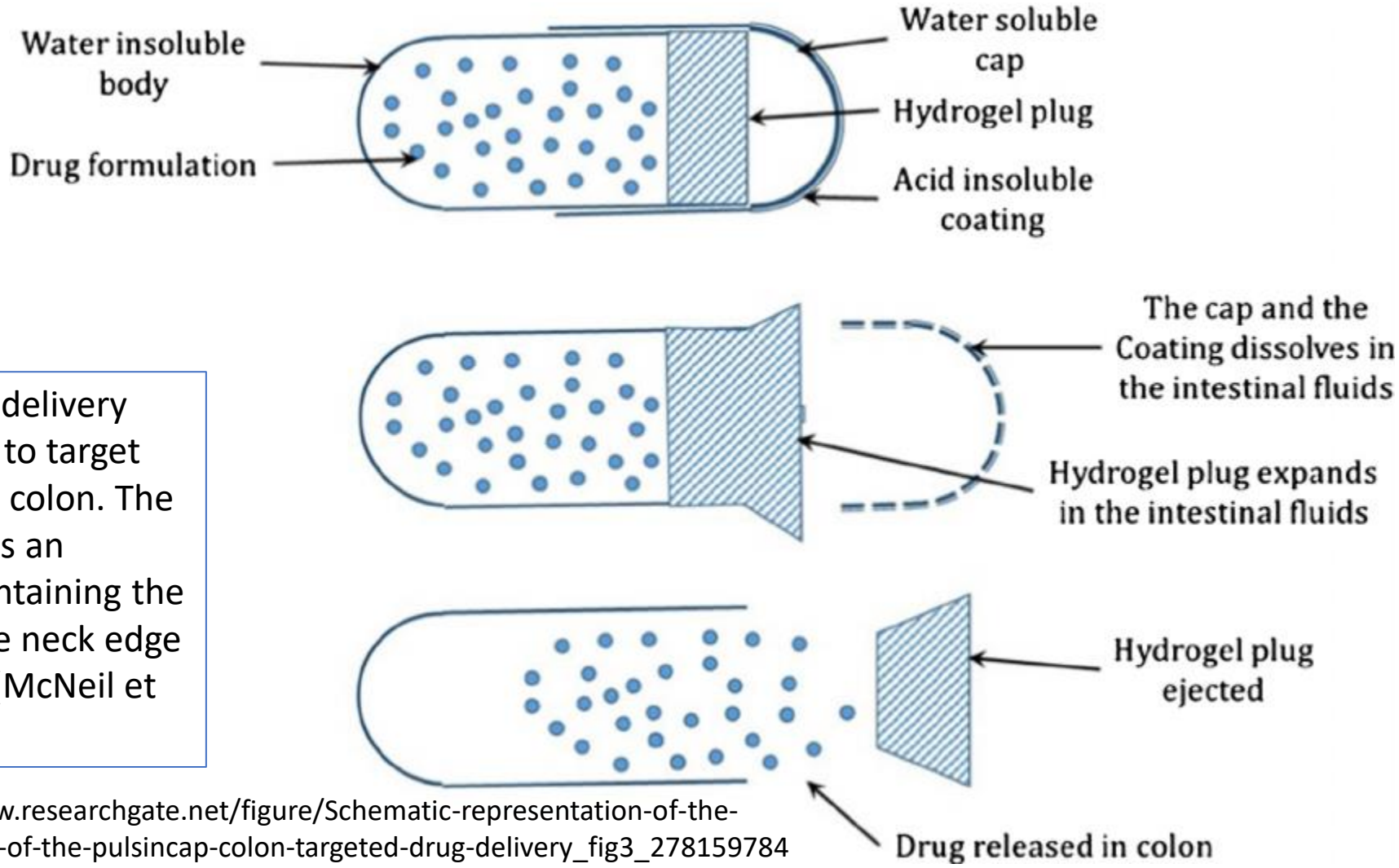
Table 2

Criteria for selection of drugs for CDDS

Criteria	Pharmacological class	Non-peptide drugs	Peptide drugs
Drugs used for local effects in colon against GIT diseases	Anti-inflammatory drugs	Oxyprenolol, Metoprolol, Nifedipine	Amylin, Antisense oligonucleotide
Drugs poorly absorbed from upper GIT	Antihypertensive and antianginal drugs	Ibuprofen, Isosorbides, Theophylline	Cyclosporine, Desmopressin
Drugs for colon cancer	Antineoplastic drugs	Pseudoephedrine	Epoetin, Glucagon
Drugs that degrade in stomach and small intestine	Peptides and proteins	Bromophenaramine, 5-Flourouracil, Doxorubicin	Gonadoreline, Insulin, Interferons
Drugs that undergo extensive first pass metabolism	Nitroglycerin and corticosteroids	Bleomycin, Nicotine	Protirelin,sermorelin, Saloatonin
Drugs for targeting	Antiarthritic and antiasthamatic drugs	Prednisolone, hydrocortisone, 5-Amino-salicylic acid	Somatropin,Urotoilitin

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3215502/

Pulsincap



This is a timedelayed pulsatile delivery system that can be configured to target drug release specifically to the colon. The time-delayed system comprises an impermeable capsule body containing the drug formulation, sealed at the neck edge with a hydrogel polymer plug (McNeil et al. 1992

https://www.researchgate.net/figure/Schematic-representation-of-the-mechanism-of-the-pulsincap-colon-targeted-drug-delivery_fig3_278159784

Erythrocyte Drug Delivery System

EDDS

- biocompatible
- Biodegradable
- Waktu paruh yang Panjang di sirkulasi
- Dapat diberi muatan substansi biologi aktid yang bervariasi

- Carrier erythrocytes are prepared by collecting blood sample from the organism of interest and separating erythrocytes from plasma. By using various physical and chemical methods the cells are broken and the drug is entrapped into the erythrocytes, finally they are resealed and the resultant carriers are then called "resealed erythrocytes".
- Surface modification with glutaraldehyde, antibodies, carbohydrates like sialic acid and biotinylation of loaded erythrocytes (biotinylated erythrocytes) is possible to improve their target specificity and to increase their circulation half-life.
- Upon reinjection the drug loaded erythrocytes serve as slow circulation depots, targets the drug to the reticuloendothelial system (RES), prevents degradation of loaded drug from inactivation by endogenous chemicals, attain steady state concentration of drug and decrease the side-effects of loaded drug. Nowadays, Nanoerythrosomes based drug delivery systems have excellent potential for clinical application.

- https://pubmed.ncbi.nlm.nih.gov/18220819/#:~:text=In%20the%20present%20scenario%2C%20amongst,variety%20of%20biologically%20active%20substances.

- Obat berada di dalam eritrosit
- Modifikasi pada permukaan eritrosit meningkatkan spesifisitas target dan waktu paruh sirkulasi
- -mencegah degradasi kimia endogen, menurunkan efek samping obat

Keuntungan dan Kerugian

Keuntungan	Kerugian
Biodegradable secara alami	Kebocoran yang cepat untuk substansi enkapsulasi tertentu
Isolasi eritrosit cukup mudah dan jumlah obat yg cukup besar dapat dienkapsulasi di sejumlah kecil volume	Beberapa molekul dapat merubah fisiologi dari eritrosit
Bahan obat tidak perlu modifikasi kimia	Encapsulated erythrocyte mungkin dapat menyebabkan variasi yang melekat pada muatan dan karakteristiknya krn sejatinya adalah biological origin
Non imunogenik dan dapat bertarget di jaringan atau organ yang sakit	Kontrol yang ketat diperlukan untuk pengumpulan dan penanganan eritrosit
	Kemungkinan kontaminasi karena asal darah, peralatan yang digunakan dan lingkungan pemuatan

https://www.researchgate.net/figure/General-mechanism-of-resealed-erythrocytes_fig2_337077362

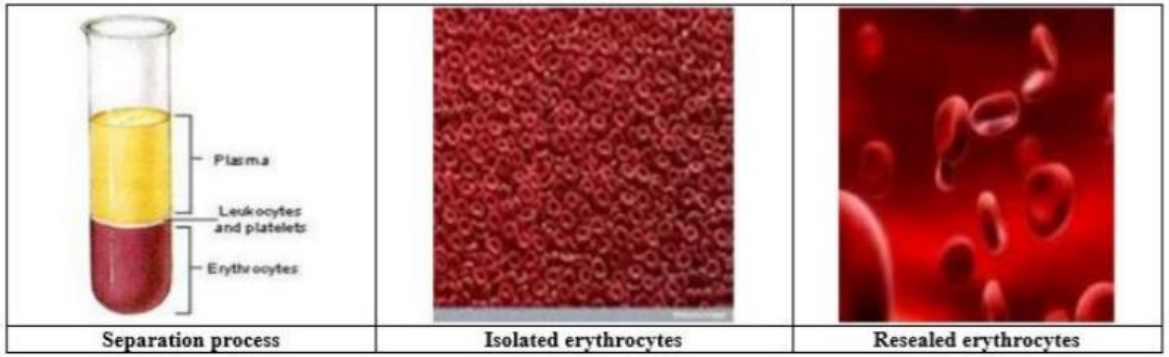
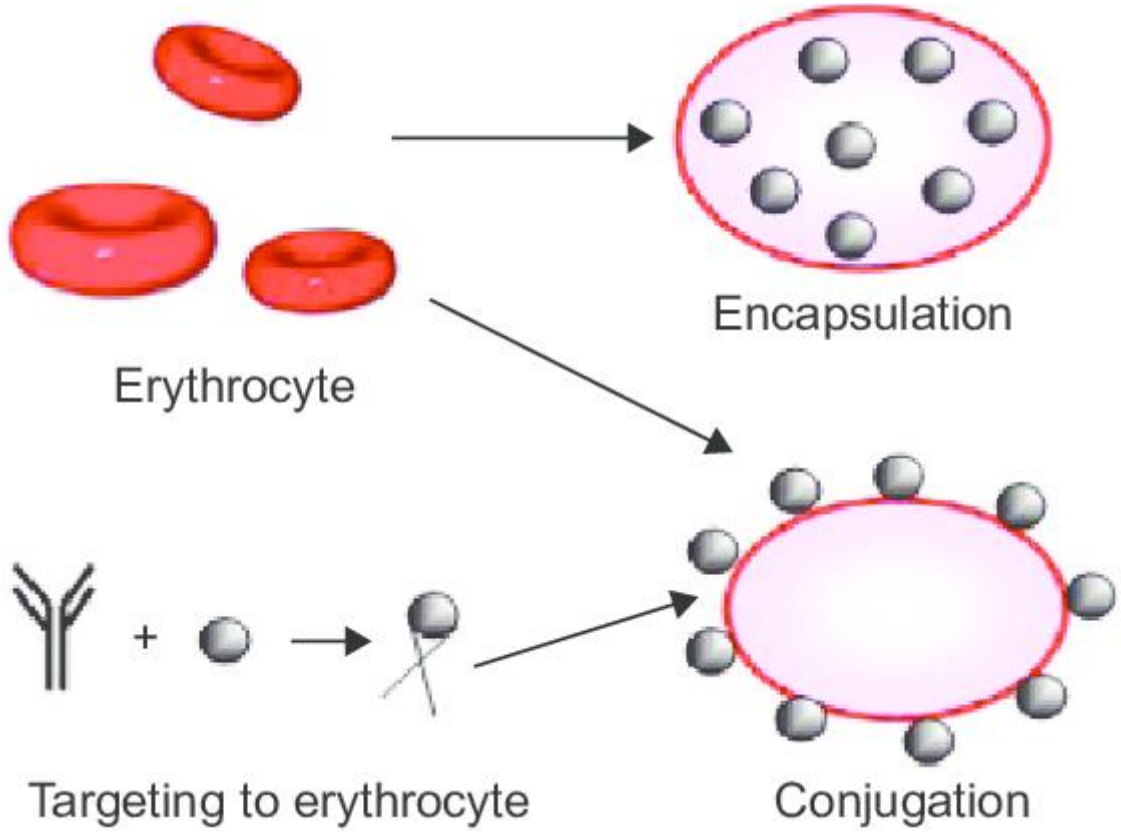


Fig3: isolation of erythrocytes

1.7 Methods (Methods of drug loading in erythrocytes)[11-15]

Several methods can be used to load drugs, enzymes or other bioactive compounds in erythrocytes. Irrespective of the method used, the optimal characteristics for the successful entrapment of the compound requires the drug to have a considerable degree of water solubility, resistance against degradation within erythrocytes, lack of physical or chemical interaction with erythrocyte membrane, with well-defined pharmacokinetic and

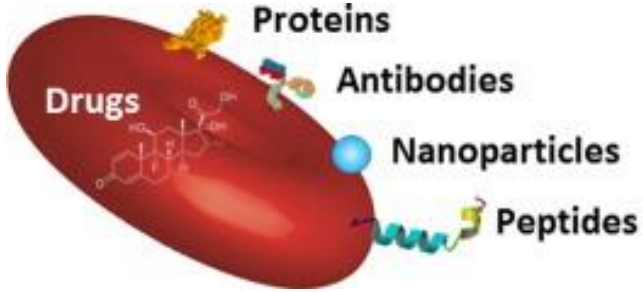
- Various types of mammalian erythrocytes have been used for drug delivery, including erythrocytes of mice, cattle, pigs, dogs, sheep, goats, monkeys, chicken, rats and rabbits.
- To isolate erythrocytes, blood is collected in heparinized tubes by venepuncture



Two main strategies of preparing erythrocytes as drug delivery systems. Notes: in the method of encapsulation, therapeutic agents are inserted within erythrocytes, while in the method of conjugation, they are attached to the erythrocyte membrane.

https://www.researchgate.net/figure/Two-main-strategies-of-preparing-erythrocytes-as-drug-delivery-systems-Notes-in-the_fig1_303322059

Aplikasi:



Sciencedirect.com

- EDDS enzim
- EDDS obat
- EDDS obat dengan target tertentu :
  - reticuloendothelial system : Sistem retikuloendotelial adalah sistem didalam jaringan dan organ berfungsi memakan (fagosit) benda asing dan bakteri yang masuk ke dalam tubuh.
    - target ke liver : tumor liver, penyakit parasite, menghilangkan toksin, dll

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