Advantages of liposomes as drug carriers for injectable drugs:

1. They are made of phospholipids mainly which is biocompatible, biodegradable & not immunogenic.
2. it can carry both hydrophobic & hydrophyllic drugs. This is important for registeration since no chemical modification of drug is required before incorporation. Carrying hydrophobic drugs is considered a form of solubilization of drug in aqueous med.
3. drug entrapped inside the liposome is separated from the surrounding medium as long as the liposome remains intact. this can protect the drug from enzymatic degradation (as in case of cytarabine)
4. drugs entrapped inside the liposome will follow the fate of liposome in the body, & the drug will be released at site of liposome destruction. in this way drug will be delivered to tissues not reached in sufficient conc. by the drug alone. in this way also, drug toxicity to specific tissue exhibited by drug alone will be decreased. (pharmacokinetic parameters are altered)

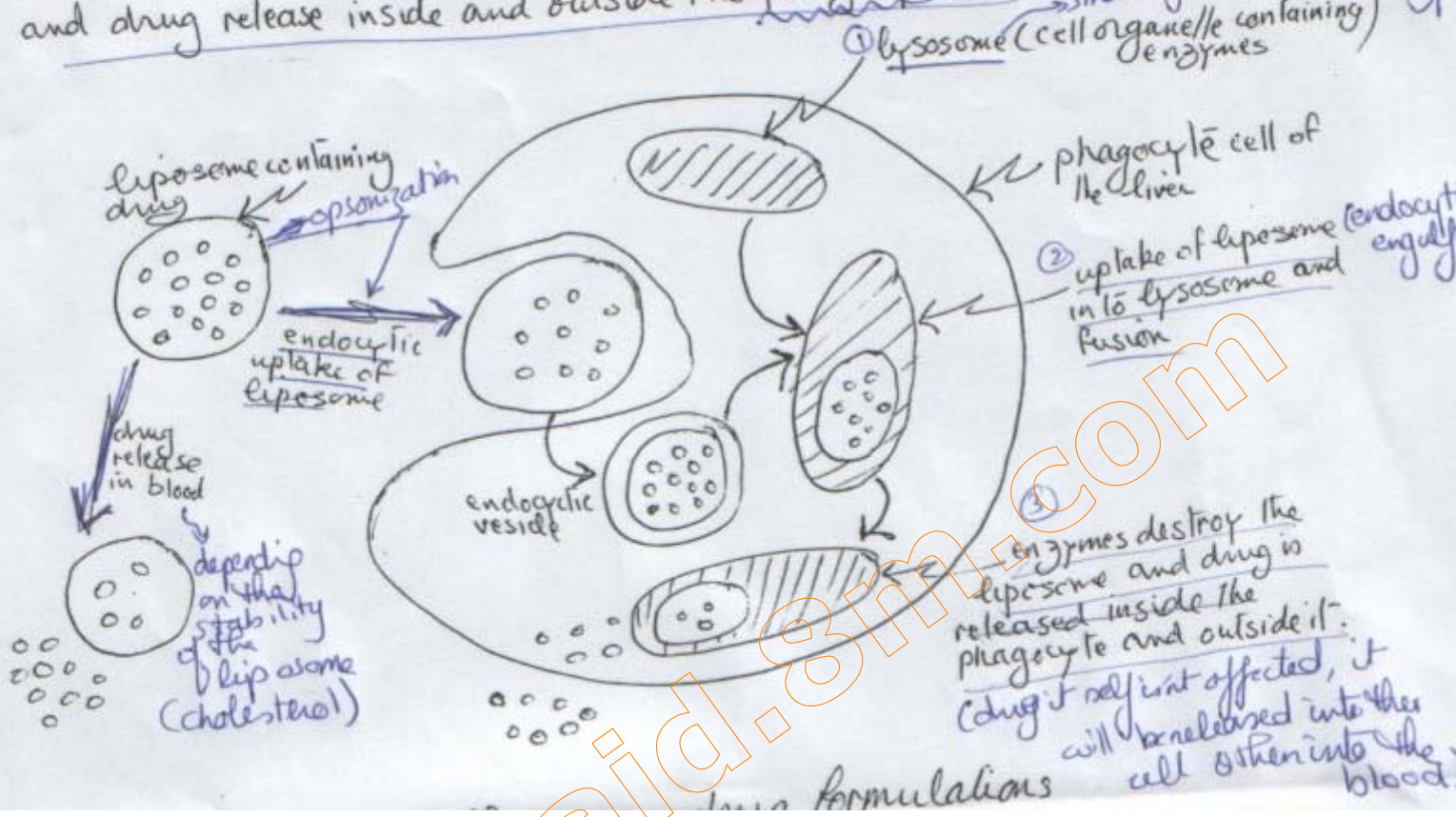
Fate of liposomes after I.V. administration:

- drug is released in blood following rapid or slow destruction of liposomes in blood (liposomes will not be stable in blood, if they don't contain enough cholesterol)
- liposomes are taken up by RES & drug is released inside phagocyte & can target adisease in liver (or can be a source of slow release of drug back to blood. (if drug is extensively metabolized by liver it will not undergo this mechanism)
- liposomes can be prepared such that they are not taken up by RES but circulate in blood for a long time giving chance for drug uptake into vascular tumors

liposome: small globule containing lipid

e- Fate of liposomes after i.v. administration

The following drawing represents uptake of liposomes into phagocytic cell and drug release inside and outside the phagocytic cell



formulations

Pharmacokinetics of liposome drug formulations:

1. they can be as conventional drugs
2. they can have same pharmacokinetics as liposome
3. they may have a very long half life if they are added to long circulating liposomes.

Differences between toxicity profile & side effects of doxorubicin & daunorubicin liposomal injections compared to conventional injections in AIDS patients w/ Kaposi's syndrome

1- Myelosuppression with neutropenia (present in both ## to the same degree)
2- nausea, vomiting, alopecia (less in liposomal ## compared to conventional)
3- extravasation effects (vesicant effects, blisters, injury at injection site) → much less in liposomal treatment.
4- potential cardiotoxicity. → very little in liposomal treatment

Effects of reduced toxicity on dosage regimen of doxorubicin & daunorubicin in liposomal formulation

- in conventional doxorubicin inject., it develops irreversible cardiomyopathy & its cumulative lifetime dose is 450-500 mg/meter²/lifetime.
- in pegylated liposomal doxorubicin inject., it is active against ovarian & breast cancer without dose limiting myelosuppression & cardiac toxicity with a cumulative dose 550-850 mg/m²/life.

* liposomal amphotericin → dose → 5 mg/kg/day
conventional « (fungizone®) → 0.7-1.5 mg/kg/day

liposomal amph. is less toxic than conventional but ~~have~~ adverse effects occur with both.

liposomal cause higher incidence of diarrhea, vomiting while chills, elevated serum creatinine, hypokalemia are less frequent w/ the liposomal product.

(liposomal AmpB inc. adherence of drug to membrane of fungus)

Sterilization of liposomal drug products:

- phospholipids are thermolabile & sensitive to heat, radiation, chemical sterilizing agents.
- The method available is filteration, but not suitable for liposome size > 0.2 μ, & it can't remove viruses.
- Some studies show that it can be autoclaved.

Stability of liposomal drug product:

- liposomes undergo → physical degradation → drug leakage
  - Coalescence problem of liposomes.
  - (That why they are supplied as lyophilized powder) → AmBisome®
- chemical degradation
  - hydrolysis of ester bond of phospholipid.
  - Oxidation of unsaturated acyl (R) chain.

Routes of administration of liposome products:

1- I.V
2- Topical : cosmetics
3- Eye drops (under investigation), it has a prolonged effect bec. it binds to corneal surface.
4- Inhalation (under investigation)
5- Oral. not suitable due to degradation of liposomes by lipases & bile salts.
6- Intraperitoneal
7- Intrathecal (long acting) e.g (DepoCyt®)
8- Buccal spray (for vitamins & nutrients)

The end of liposomal based Pharmaceuticals