‘‘ Improvement & innovation trends in lipid based drug delivery system ’’

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ABSTRACT

Bioavailability defined according to Food and Drug Administration (FDA) that "the rate and extent that which the active drug ingredient(API) and therapeutic moiety is absorbed from a drug product & becomes available at the site of drug action, Because in practice bioavailability is rare that drug concentrations can be determined at the action site, . now a day the (LBDDS) Lipid-based drug delivery systems has have shown the effective size dependent properties of the drug so the (LBDDS) have attracted a lot of attention. The LBBDS have advantages of higher degree of biocompatibility and versatility. This LBDDS systems are commercially viable to the formulate of pharmaceuticals product for the topical, oral, pulmonary, or parenteral delivery use. These Lipid formulations can be modified in different ways that meet a wide range of product that are requirements as per the , route of administration, disease condition, and cost product stability, toxicity, and efficacy. Bioavailability of Drugs Improvement In the CD complex formation The bioavailability of the drug can be enhanced. It can be attained by enhancing the drug available at the surface of the biological barrier of drug like eye cornea, mucosa or skin. where the drug improvement partitions into the membrane without the disturbing the lipids contained in the barrier of the drug . The bioavailability active of drugs depends on parameters such as drug dissolution rate solubility and intestinal absorption rate.

INTRODUCTION

As per the United State Food and Drug Administration (FDA) term the bioavailability as "the rate and extent that which the active drug ingredient(API) and therapeutic moiety is absorbed from a drug product & becomes available at the site of drug action, Because in practice bioavailability is rare that drug concentrations can be determined at the action site [1]. It is defined as "the rate and extent that the active drug is absorbed from a dosage form and becomes available in the systemic circulation." The bioavailability refers as the absorption of a drug from the gastrointestinal tract(GIT)by following the oral administration of a dosage form. The dosage form may be any type of product, including a solution, suspension, tablet, capsule, powder, or elixir. It can also refer to as other types of dosage form, such as intramuscular injections, ointments and other topical preparations, transdermal patches, and implants, which also require an absorption step prior to reaching the systemic circulation. The drug administration in the intravenous route result as 100 % bioavailability, at which the amount of drug reaching at the systemic circulation which is equal to the total administered dose [2] The word Bioavailability, one of the principal pharmacokinetic properties of drugs, is used to describe the fraction of an administered dose of unchanged drug that reaches the systemic circulation. The measurement of the amount of the drug in the plasma at periodic time intervals indirectly indicates the rate and extent at which the active pharmaceutical ingredient is absorbed from the drug product and becomes available at the site of action. Bioavailability is one of the essential tools in pharmacokinetics, as it must be considered when calculating dosages for non-intravenous routes of administration. It is expressed as either absolute or relative bioavailability [3] In lipid-based drug delivery systems many significant efforts have been applied to use the potentials, as this provides the suitable term of site specific as well as time controlled delivery of drugs with different molecular weight, it is smaller or larger, and also the bioactive agents [4, 5]. main challenges for the formulation of Poorly water-soluble drugs as scientists with regard to solubility of drug and bioavailability of the drug. The (LBDDS) Lipid-based drug delivery systems have shown the effective size dependent properties of the drug so the (LBDDS) have attracted a lot of attention. The LBBDS have advantages of higher degree of biocompatibility and versatility. This LBDDS systems are commercially viable to the formulate of pharmaceuticals product for the topical, oral, pulmonary, or parenteral delivery use. These Lipid formulations can be modified in different ways that meet a wide range of product that are requirements as per the , route of administration, disease condition, and cost product stability, toxicity, and efficacy. The Lipid-based carriers are safe and efficient , they also been proved to be attractiveness for the formulation of pharmaceuticals, as well as vaccines, diagnostics, and nutraceuticals [6]

Advantages of LBDDS [7]

(1) controlled release of drug and targeted release of drug.
(2) Pharmaceutical stability of the drug substance.
(3) The drug content is High and enhanced as compared to the other
Carriers drug delivery system.
(4) practicability is carrying both hydrophilic and lyophilic drugs.
(5) Biocompatibility and Biodegradability is good .
(6) Excipients are versatility.

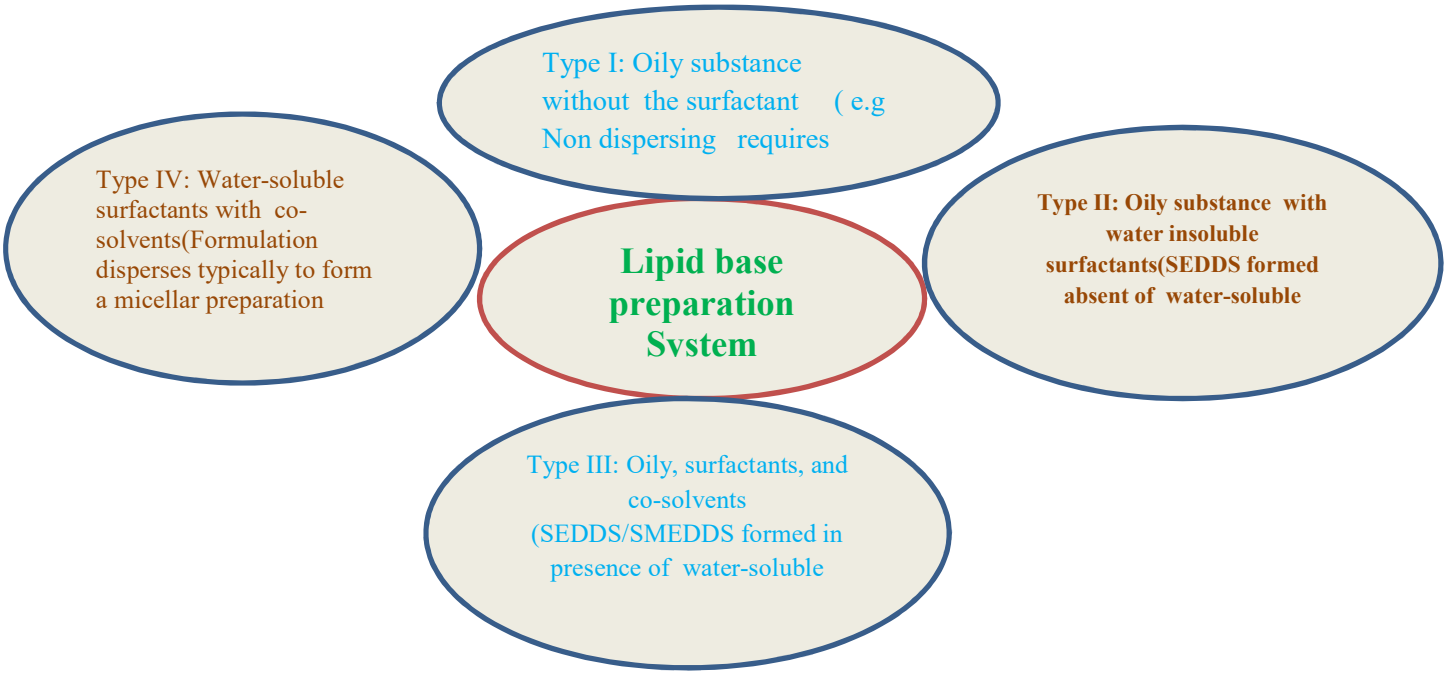


Table -1(lipid formulation classification system)(8)

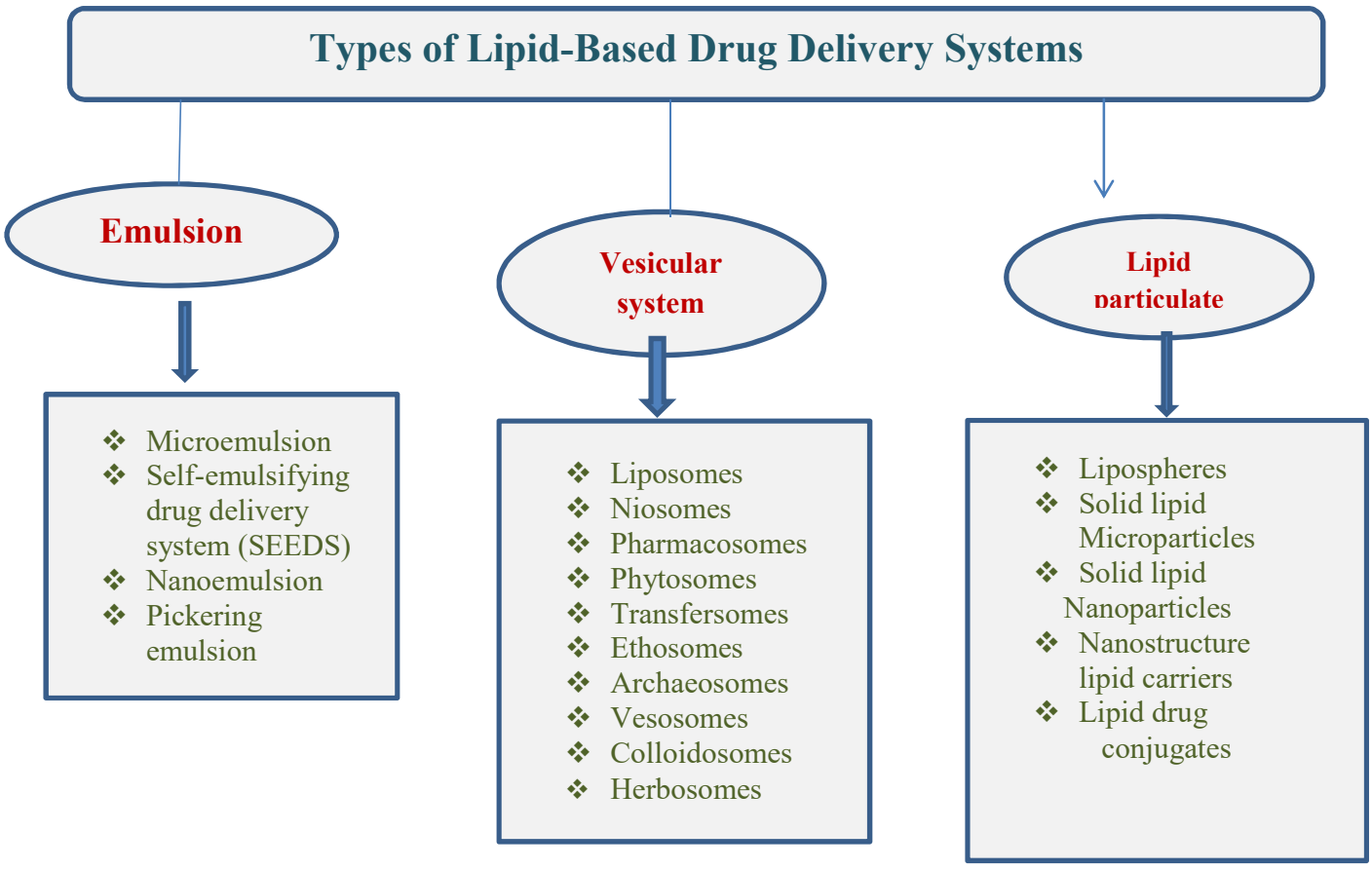


Table 2 (Types of Lipid-Based Drug Delivery Systems)(9)

Recent drug delivery systems and their uses and advantages, and disadvantages.

Sl.no	Recent Drug Delivery System	Advantages of DDS	Disadvantages of DDS	Therapeutic Use of DDS
1.	Camouflaged Of RBC(Red Blood Cell) Membrane-Micromeritics Nanoparticles Drug Delivery System	Immune system triggering are avoided and long-term circulation is achieves . Inherent Biocompatibility Inherent The Biodegradability Is avoid which accumulation related the toxicity.	At Being camouflaged in the part of the system(biological), Regulation may arise complex issues & protein purification ,identification and conjugation may be by passed.	The coated of erythrocyte membrane-micro-formulations have been applied in antitumor and anticancer research to substantial accomplishment(10,11,12)
	Hexagonal Boron Nitride Nano sheet Drug Delivery System	Bio inertness, very little to no level of toxicity, high drug-loading ability	Hydrophobicity makes it challenging to function in a biological system	Used in tumor labeling and sensing(13)
2.	Hyaluronic Acid-Based(HAB) Drug Nano Carriers Drug Delivery Systems	Good biocompatibility, biodegradable and non-immunogenicity, it has the ability to recognize over-expressed cells and kill them	They may increase cell proliferation when they interact with certain protein receptors, potentially hazardous to cancer patients	Cancer chemotherapy(14,15)
3.	Polymer-Lipid Hybrid Nanoparticles Drug Delivery System	In encapsulation Physical stability is good and biocompatibility, in vivo cell delivery efficacy	Drug entrapment is Poor and loading capacity, Inflammation and damage of tissue can affect or inactivated the lipids in serum	Targeted in the anticancer therapy(16,17,18)
	Micro Electro Mechanical Systems For Drug Delivery	Drug loading capacity is high , bioavailability, precise drug delivery, efficient and it is less	It Requires repeated surgeries for refilling of the drug.	Heart-related disorder , As contraceptives in women(19,20,21)

		painful		
	Delivery System In-Situ Gel Drug	patient compliance Increased, reduction of number administrations, Bioavailability is increased , controlled and sustained release of the drug.	Only low dosage of drug can be given, eating and drinking may be restricted after administration of drug for a few hours, stability is low due to chemical degradation, it require more fluid	Employed in rhinitis, used to reduction in the ocular intolerance in Glaucoma , and reduction in the insulin permeation interactions.(22,23)
	Self-Micro emulsifying Drug-Delivery System	Poor Bioavailability & solubility drugs, Stability long duration, protection of sensitive drug materials, availability of the solid and liquid forms of drugs.	Interaction of drugs it could be potentially accelerate the physical aging in patients due to interactions of glyceride and oxidation of the vegetable oil.	Used in the pulmonary infections treatment (24,25)
	Approach of Combination of drug delivery .	Loading capacity More and efficacy, rate increased , sustained release of drug , cytotoxicity, and immunogenicity are limited	The patient compliance could be low , fixed dose ratio for inflexible, incompatibility of pharmacokinetics properties , increased the rate of toxicity	Used in Chemotherapy and hypothermia Therapy(26,27,28)
	Targeted Drug Delivery System	Side effects Reduced and Rate of Efficacy high , liver metabolized the materials and kidney Those reduce the level of toxicity.	Productivity cost high , immunogenicity, and non-specificity of the targeting ligand, can be easily clearance from the blood	Tumor related Dis order, Cancer therapy (29.30.31)

Bioavailability of Drugs Improvement

In the CD complex formation The bioavailability of the drug can be enhanced. It can be attained by enhancing the drug available at the surface of the biological barrier of drug like eye cornea, mucosa or skin. where the drug improvement partitions into the membrane without the disturbing the lipids contained in the barrier of the drug . The bioavailability active of drugs depends on parameters such as drug dissolution rate solubility and intestinal absorption rate.

In the formation of inclusion complex improves in the dissolution rate, and solubility in gastrointestinal fluids, then increases in the amount of drug in blood. In the other side , the

time required to dissolve the drug from solid form to the gastrointestinal fluids and reduced in the diffusion to blood circulation.

The Different mechanisms for enhancing the bioavailability have been identified of active drugs. It should be including

(1) improving in the drug solubility and drug dissolution rate,

(2) prevent the degradation of chemically unstable drugs in the gastrointestinal tract.

(3) Improve the permeation of proteins and peptide through the nasal and rectal mucosa by modifying membrane fluidity;

(4) compounds like Bile acid, cholesterol, lipid. may act as competitive guest molecule to inclusion the complex with CD, improve in the drug release.

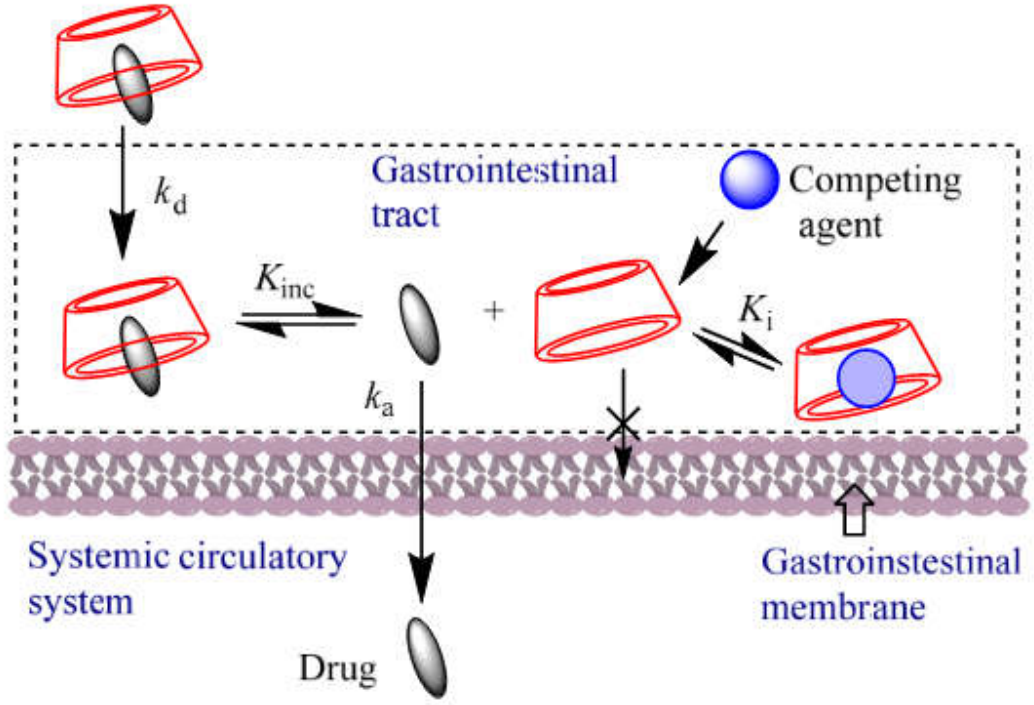


Table-3(Representative process to release a lipophilic drug.)

k_d K_{inc}, K_i, and k_a are stand for the dissolution rate constant, the inclusion constant of the complex of the CD with the drug are inclusion with constant of the drug complex of the CD with the competing agent, and the absorption rate is constant, respectively.

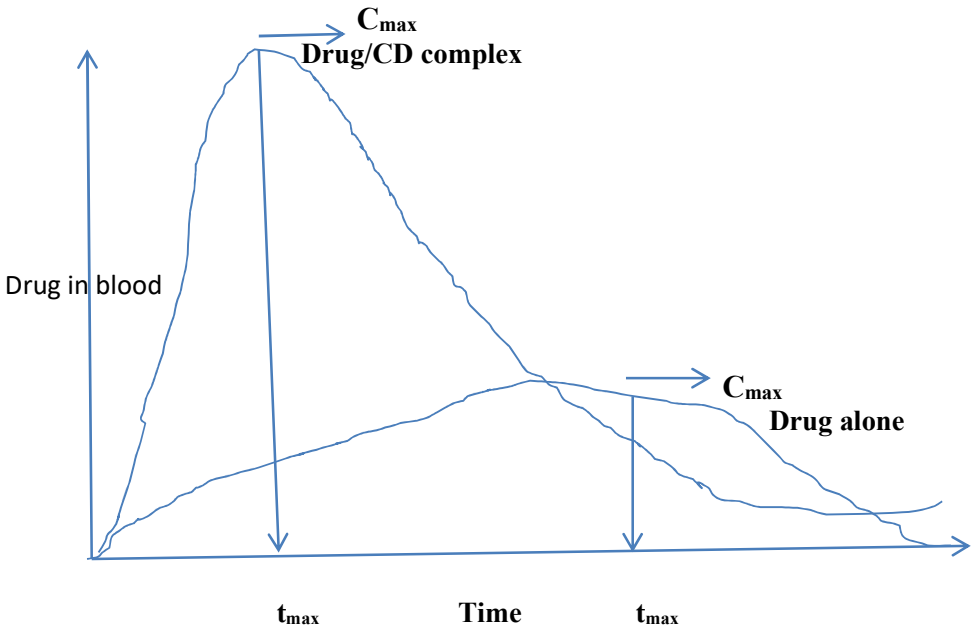


Table-4(Enhancement in the bioavailability of a drug by an inclusion complex formation.)

The Representative dynamic of equilibrium of self-assembled cyclodextrin nanoparticles and drug permeation into the ocular surface by the concentration gradient. Kinc and KS stand for the Figure 4. Representative dynamic equilibrium of self-assembled cyclodextrin nanoparticles and drug permeation into the ocular surface by the concentration gradient. Kinc and KS stand for the inclusion the constant for the drug-cyclodextrin (D-CD) complex and for the equilibrium constant for the self-assembled cyclodextrin nanoparticles. Adapted from[32].

Improvement of the Safety and Stability of Drugs

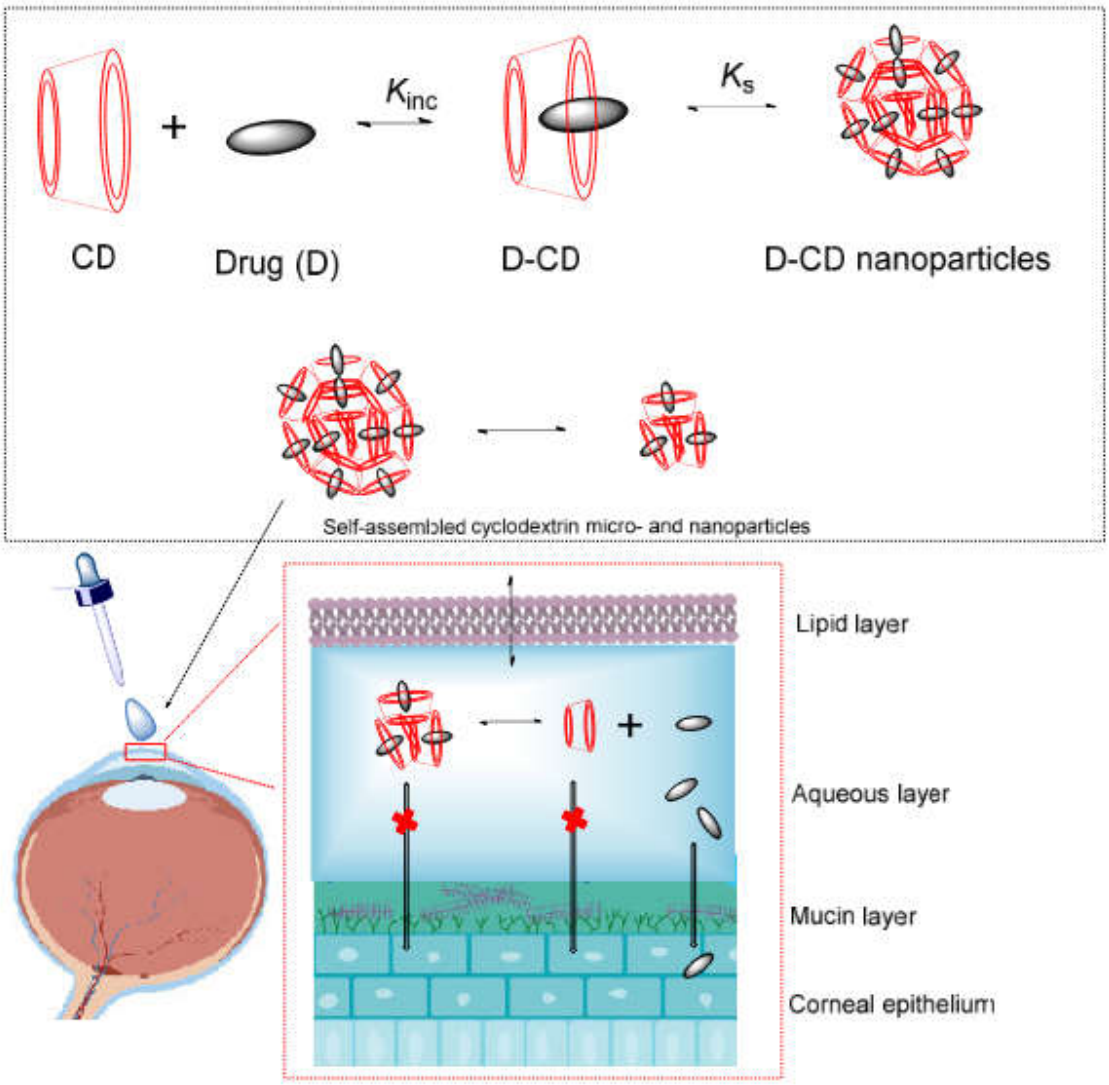
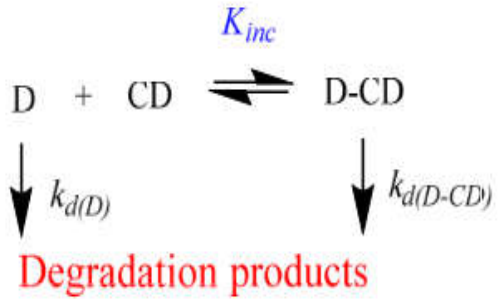


Table -5

Improvement of the Stability and Safety of Drugs

Ds have a key role in the chemical stability of active drugs, retarding or accelerating different types of reactions such as hydrolysis, isomerization, dehydration, and oxidation. For an inclusion complex of stoichiometry 1:1 (D-CD complex, Equation (2) where kd(D) and kd(D-CD) are the observed rate constant for the decomposition of free drug and of the D- CD complex, respectively). In a variety of reported studies, kd(D-CD) < kd(D) and the formation of D-CD complexes improve the stability of the drug [33]. Note that the phase-solubility studies are

addressed in drug-saturated media, i.e., in non-ideal conditions, and the presence of other excipients, such as buffer salts, polymers, and preservatives, can change the complexation efficiency. Therefore, the complexation media during the formulation of the drug should be similar to the composition of the final formulation .[34].



Absorption Mechanisms of Liposomes

Oral liposomal formulations must pass through the intestinal epithelium before entering the systemic circulation. Despite all the disruptive conditions, liposomes can pass through the intestinal epithelium through various absorption mechanisms (Figure 6). Enterocytes lining the small intestine are primarily responsible cells for drug absorption in the gastrointestinal tract. After passing through the mucus layer in the intestine, the drug molecules must pass through the glycocalyx and reach the epithelial layer. Transport through the epithelium occurs via the paracellular or transcellular pathways [35].

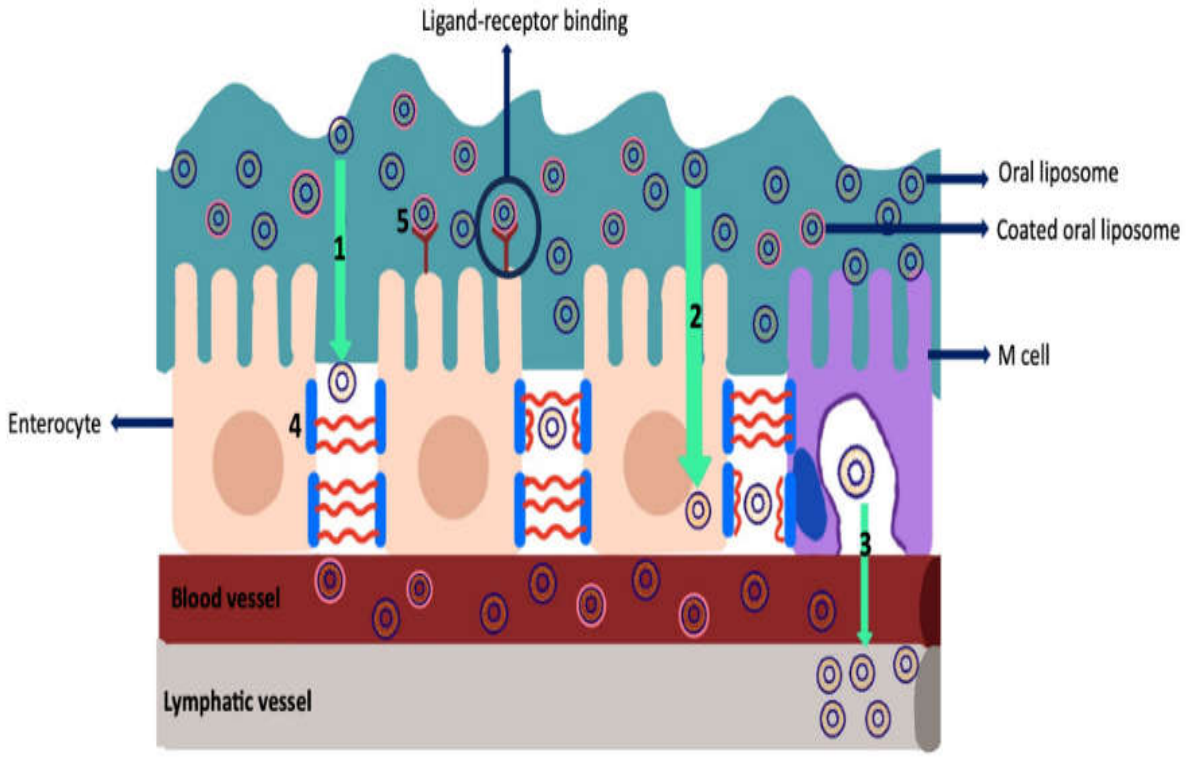


TABLE-6(Schematic representation of the passage of oral liposomes from the intestinal environ-ment into the circulation. (1) Paracellular pathway, (2) transcellular pathway, (3) M cell-mediated transcytosis, (4) tight junction, (5) receptor-mediated endocytosis)

SL.NO	Surface Modifier	Function
	PEGylation	- Increase the stability - Increase the residence time in the body - Increase drug stability - Increase the absorption rate for oral administration[36]. Increase drug penetration and accumulation rate in cells[37] - Increase resistance to digestive enzymes[38] - Increase drug-loading capacity[39] - Drug release control[40] - Decrease particles aggregation[41]
	Block co-polymer	Increase the stability [42] - Increase the residence time in the body[43] - Increase the cellular uptake and targeting ability[44]
	Chitosan coating	- Increase the stability of LNPs - Increase the residence time in the body - Increase the absorption rate for oral administration - Increase mucosal adhesion[45]

		- Increase delivery to the lungs via inhalation[46] - Increase drug delivery to brain[47] - Increase permeability to corneal cells[48] - Increase skin penetration[49] - Increase intracellular penetration[50] - Increase sustained release time[51]
	Surfactant protein	Increase the structural stability of the membrane [50] - Increase resistance to various environmental stress (i.e., ion, pH, and temperature) - Antibody conjugation for increasing targeting ability of LNPs based on non-chemical treatment through genetic modification[51]

Current Research and Trends in LBDD

Using of the plant-based bioactive compounds Novel drug delivery technologies have been developed to reduce or eliminate limitations, nanotechnology involves the engineering and production of materials at the atomic and molecular levels, which there are allow the various options in drug rout administration by enhancing therapeutic effectiveness ,herbal technology developed through the nano technology by present of various unique advantages that included the ability to transform poorly soluble and inadequately absorbance as the stabilize volatile ingredients within the effective pharmaceutical delivery system based on nanotechnology opportunities to enhanced the efficacy of herbal treatment and therapy [52]

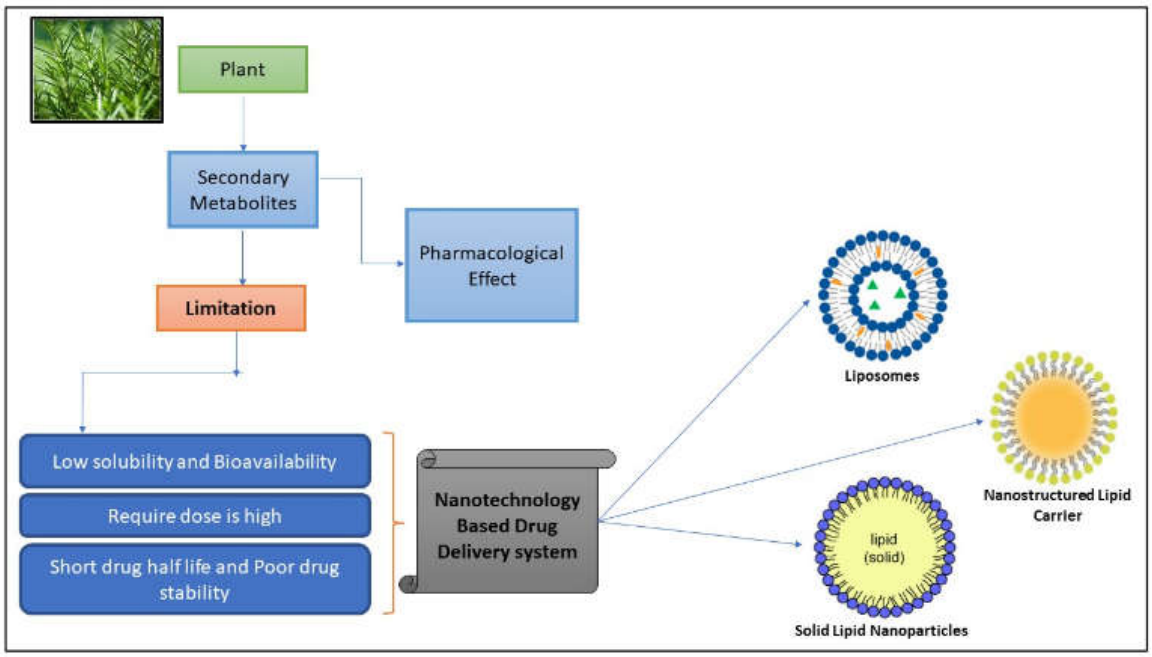


Figure 1. Diagram illustrating the flaws of bioactive compounds with their problem and solution.[52]

Both hydrophobic and hydrophilic bioactive compounds have been successfully delivered using lipid-based nanoparticles, including liposomes, phytosomes, SLNs, and NLCs in clinical trials[53,54]

CONCLUSION

Nano medicine has developed impressive progress in modern targeted therapy against many diseases. Applications of nano technological strategies to drug and vaccine delivery has improved not only the effectiveness, selectivity, duration, but also bio distribution of conventional drug carrier systems. Furthermore, the continual efforts in synthesis and screening of functionalized LNPs by chemically optimizing their molecular structures and in vivo biodegradability would promote the development of more versatile, highly efficient, and biocompatible delivery vehicles.[55]

LNPs with complex structures are being designed to overcome biological barriers specific to individual patient as demanded by precision medicine. Modified nano carrier designs are adapted by patient data and engineered to permeate particular barriers may enhance the delivery and response to precision therapies. LNPs hold

great promise Engineering therapy and editing, vaccine development, oncology and other genetic medicine.[56]

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