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ISSN: 2157-7439
Journal of Nanomedicine & Nanotechnology

Review Article

New Deliveries Used to Enhance Bioavailability through Novel Drug Delivery Systems

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ABSTRACT

Novel Drug Delivery System (NDDS) is the most recent strategy aiming at overcoming the issues belying drug bioavailability. It refers to the degree and scope to which drugs are made accessible to the specific tissue after the administration of the drugs. Majority of the drugs utilized nowadays have reduced bioavailability, therefore they require administration at higher dosage because small portion of administered dosage of it is taken into the body system flow through the body's systemic circulatory units to get to the major targeted site. The outcome is large wasted portion of major quantity of drugs which will definitely lead to side effects. Pharmaceutical knowledge principally looks forward to improving and quickening permeability and solubility of low bioavailability drugs. Nanotechnology refers to an idea introduced into NDDS which allows weight lessening of the constituent parts of drugs related to increase in strength as well as enhanced functionality. Different techniques like nanosuspensions, niosomes, liposomes, nanoemucubosomes, lsions, Solid Lipid Nanoparticles (SLN), Nanostructured Lipid Carriers (NLC), phytosome, cyclodextrins etc. are adopted for enhancing bioavailability. The current work concentrates on the various techniques adopted for use for bioavailability quickening with their adverse effects and the merits attached to their uses.

Keywords: Bioavailability enhancement; Novel drug delivery systems; Solubility

INTRODUCTION

The bioavailability of medicines could be quickened using new drug administration system *via* transporting the medicine to the specific site of action [1]. Therefore, the effect it has on the targeted tissues as well as the adverse side effects on that site will be minimal; while the storing of the therapeutic mix in the main tissues will increase. Furthermore, the appropriate dosage of the drugs will be reduced at the predetermined rate. Current advancements in nanotechnology show that nanoparticles or structures that are less than 100 nm in sizes are strong drug carriers. Such nanostructures show special physicochemical as well as biological characteristics the capability to quicken reactive zone as well as cross tissue barriers and cells. The reason for this is because of their tiny sizes making them the best material for application processes in biomedical science [2].

Nanoparticles are known to have large surface region to volume proportion, which signifies that more areas are exposed to reaction leading to higher suspension of nanoparticles in the solution, leading to more of bioavailability, lesser drug dosages as well as reduced toxicity. In long established drug administrative techniques like intravascular or oral administrative method, the therapeutic molecules or medicines are circulated all through the body *via* universal blood movement. Therefore, many molecules mix their targeted regions, which will result into remaining in the bloodstream to cause health issues. The medicine as well as the therapeutic components have stunted plasma half-life, serum instability, immunogenicity power and are insoluble in water. Owing to this, there is rapid clearance of the MPS or "mononuclear phagocytic system" and their efficiencies are limited simultaneously. Bioavailability is the degree at which practical moiety or drugs or metabolites penetrate the circulatory system to access the action sites [3].

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Received: 27-Jun-2019, Manuscript No. JNMNT-24-29; **Editor assigned:** 02-Jul-2019, PreQC No. JNMNT-24-29 (PQ); **Reviewed:** 16-Jul-2019, QC No. JNMNT-24-29; **Revised:** 01-Aug-2024, Manuscript No. JNMNT-24-29 (R); **Published:** 29-Aug-2024, DOI: 10.35248/2157-7439.24.15.747

Citation: Ali HS (2024) New Deliveries Used to Enhance Bioavailability through Novel Drug Delivery Systems. J Nanomed Nanotech. 15:747.

LITERATURE REVIEW

The novel drug delivery systems such as; niosomes, liposomes, phytosomes and others that easily penetrates into the body pre-systemic metabolism, tends to reduce the negative impact caused by the addition of medicine to the wrong areas of the body which were not the targeted zones. This will help in improving tissue macrophage circulation in patients suffering from geriatric and pediatric. It will also help to protect against chemical and physical degradation such as increasing stability, solubility, sustained delivery and permeability. The rate of dissolution of the drug could be seen from the viewpoint of Noyes-Whitney formula and it corresponds to the outside region since the particles are shortened minute sizes. Therefore, saturation solubility as well as dissolution degree of drugs whose water solubility are poor could be augmented [4].

During absorption and dissolution, the lipophilic drugs *via* oral administration forms rate limiting steps. The absorption of intestinal medicines as well as intestinal permeability could be explained properly through the Biopharmaceutics Classification System (BCS). The recent studies deal with diverse new methodologies of drug administration as the modes of quickening bioavailability insoluble drugs administration systems. Different novel drug delivery systems in drug bioavailability enhancement (Figure 1).

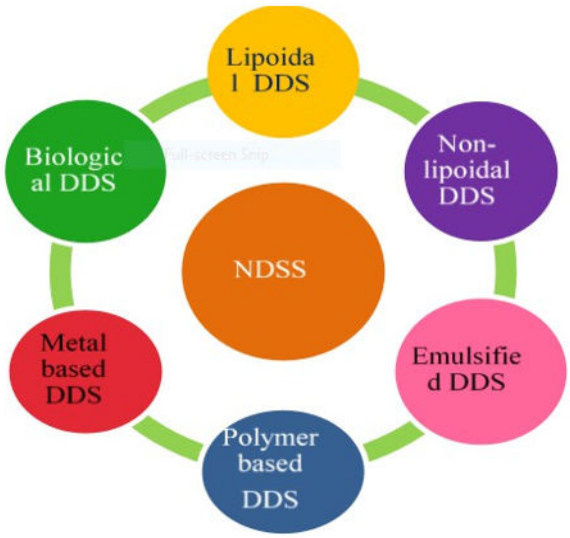

Figure 1: Classification of novel drug delivery system.

DISCUSSION

Different novel drug delivery system

Nanocarriers: Nanocarriers having optimized physicochemical as well as biological attributes are easily taken up *via* the target sites unlike when compared to large molecules. Hence, they can be used efficiently as delivery systems for the bioactive compounds which are presently available in addition to enhance the drugs bioavailability. Nanocarriers surface works by either absorbing the drugs or through a covalent attachment on its surface and encapsulation inside the nanocarriers. Covalent linkage helps in controlling the total number of molecules of drug, *i.e.*, the precise control on the amount of compound delivered or linked with the nanocarrier. Nanocarriers are used for cell-specific targeting through 2 mechanisms namely, active or the passive. The active mechanism works on the principle of drug attraction (conjugate of nanocarriers) towards the target site through recognition legends, which are linked to the conjugate antibody surface, ligands of low molecular weight such as peptides, etc. as well as by manipulating the physical stimuli such as pH, temperature, etc. Contrary to that, passive mechanism occurs due to increased vascular permeability and retention (EPR) specific for tumours with leaky tissues [5].

Drug delivery systems based on lipids-liposomes

Liposomes: Liposomes consist of a compartment which is aqueous and enclosed with a bilayer membrane made of lipid. The linkage of a lipophilic moiety of the bilayer with the non-polar part of the drugs creates a hydrophobic environment outwards. However, drugs which are hydrophilic in nature links with inner phase of the vesicle. Such diverse bypass feature as well as composition and overall construct of liposomes help to create a system which is dynamic and adaptive to enhance the solubility of drugs. The pH of the stomach and the enzymes present in the intestine and bile salts causes fast degradation of formulations of liposomes which are administered orally. The liposomal formulation of acid labile drugs such as cefotaxime helps in providing increased intestinal permeation and protects it's temporarily against the stomach acidic nature for the drug. A study has reported that human cancer treatment can be enhanced with the help of a liposomal drug delivery systems along with decreasing the toxicity of the widely used lipophilic drug, vincristine. Furthermore, the bioavailability of low solubility drugs is enhanced with the help of phospholipid-based liposomes. The *in vivo* study carried out by wisniewski suggested that up to 5 folds of enhancement in bioavailability can be made using a liposomal drug delivery system as compared to control formulation [6].

Cubosomes: Cubosomes are small-sized nanoparticles up to 100 mm to 500 mm (diameter) characterized by cavernous structures, which helps in separating the 2 aqueous channels with a huge interfacial part. The particles consist of bicontinous cubic phases that are isotropic, optical, viscous and consists of a solid like substance which is liquid crystalline and having a symmetry of cubic crystallography. Schwarz while studying cubic phases defined three different types of minimal surfaces as per curvatures. However, Takeuchi et al., suggested 3 different cubosomes structures to enhance bioavailability namely, Pn3m (*i.e.*, diamond/D surface), Ia3d (*i.e.*, gyroid/G surface) and Im3m (*i.e.*, primitive/P surface) according to nodal surfaces.

Furthermore, Wakaskar depicted the behavior of cubic phases as lamellar phases when dispersion occurs with improving shear as the elasticity increases among phases due to high oscillatory frequencies. The studies have also reported that, Cinnarizine (CZ) cubosomes which are developed from phytantriol provides long duration of effective release of drugs and also enhances the oral bioavailability up to 20 percent

in comparison with suspension of CZ (9 percent) and emulsified oleic (around 12 percent). Another study reported that cubic nanoparticles loaded with simvastatin when formulated with the help of glyceryl monolete or poloxamer 407 tend to enhance the bioavailability up to 2.4 times as compared to a micronized powder of simvastatin [7].

Self-emulsification system of drug delivery is a type of a cardinal technique to enhance the bioavailability of the drugs that have low solubility and permeability. Ni et al., evaluated in situ property of absorption of loaded with curcumin depicted a significant enhancement in the bioavailability of the drug in rats. Another study by Kabir and his co-workers suggested an enhancement in bioavailability when self-emulsifying system of dexibuprofen is prepared. The results provided evidence of significant enhancement in AUC and Cmax.

Metal-based drug delivery system-silica-based

Silica-based: Silica-based substances are found to be an effective way of drug delivery as it provides several advantages such as easy surface modification hence, providing various molecules to be enhanced, target site delivery system and low toxicity in cells and tissues. The different forms of silica materials such as xerogels and mesoporous silica nanoparticles provides benefits in terms of carrier system for drug delivery such as biocompatibility, high porous network and easy function [8]. Such types of systems have the property to be easily modified with the help of different molecules to enhance the site-specific cellular uptake. Song et al., proposed the magnetic mesoporous silica nanospheres through the incorporation of super paramagnetic nanospheres made out of Fe_3O_4 or polystyrene.

Carbon nano-substances: The nanomaterials made out of carbon are further divided into nanotubes and horns whose bioavailability can be enhanced by modifying the surface of nanomaterials using chemicals. Carbon nanotubes could be used as a drug delivery carrier in therapies such as cancer therapy as well as various therapies as it helps in the prolonged release of the drug on the target tissue and is nontoxic to healthy tissues. A research made by Sharma, suggested that when a most commonly used chemotherapy therapy drug such as paclitaxel is conjugated with chains of PEG SWNTs through an ester bond which gets cleaved when transformed into a water-soluble complex *i.e.,* SWNT paclitaxel conjugate depicted efficient role of carbon nanotubes to accumulate at the target site and enhance the bioavailability in mice [9].

Polymer-based system

Polymer-based nanoparticles: Polymeric nanoparticles are polymeric, consisting of 3 polymeric forms *i.e.,* natural, semi-synthetic as well as synthetic drug carriers. They fall in the range nano-scale-micro-scale. The most widely studied drug delivery system is poly nanoparticles. The drugs attached to the nanoparticles are divided in the hydrophobic core of the micelles and their outer layer of hydrophilic nature helps in the formation of a stable dispersion when present in an aqueous media.

They also have a property of being functionalized together with PEG to maintain the stealth property as well as target ligands on the outer surface of micelle. Furthermore, a study on bioavailability enhancement cefpodoxime proxetil, the drugs with low solubility were held in comparison with the help of natural polymers such as methylcellulose, sodium alginate, etc. On the other hand, jabbar prepared a polymeric material which is hydrophilic known as kollidon VA64, using surfactants and a plasticizer to enhance the dissolution and bioavailability of efavirenz. The study, however, concluded that the enhanced bioavailability and solubility could be obtained when PEG 4000 is used.

Dendrimer nano-carriers: Dendrimer is highly branched structures which consist of an inner core, branch series and its outer surface is covered with various functional groups. They are considered as a novel drug delivery system due to their small size *i.e.,* nanometer and ease to prepare and function them. Several studies have depicted the enhanced bioavailability level with the use of dendrimer particles such as one depicted by Zhang et al., that make use of G3 and G4 polyamidoamine based upon ethylenediamine that forms drimer when combined with grafts of monomethyl ether PEG for encapsulating the drug such as anticancer drugs namely, methotrexate. A similar study by Sethi et al., depicted that polyamidoamine dendrimers can be used to enhance the solubility of methyl (5 (propylthio)-1H-benzimidazol-2-yl) carbamate, albendazole in an aqueous solution. The study concluded that such structures help in enhancing albendazole solubility [10].

Biological drug delivery system-cyclodextrins

Cyclodextrins: Cyclodextrins are derivatives of starch and are among the most highly studied drug system to enhance the drug bioavailability, solubility, stability, as well as the rate of dissolution among drugs which shows low solubility level. The large molecules of cyclodextrin show a molecular weight of about 1000 more than over 1500 and are highly permeable in terms of biological membranes. The molecules are composed of lipophilic molecules inside the cavity while the outer cavity is composed of hydrophilic molecules which provide cyclodextrin to interact with a large number of molecules through non-covalent inclusion complexes which provide high stability, highly soluble in water, enhanced bioavailability and reduced side effects. The important property of cyclodextrins is the ability to enhance the bioavailability and the delivery of a drug through biological membranes [11].

Phytosome: They are also known as phytolipids drug delivery system which is considered as a bridge between the conventional system of drug delivery and novel system of drug delivery. It is novel technique formulated and patented by Indena for incorporation of either standard plant extractions or aqueous soluble phytoconstituents inside the phospholipids for the production of molecular complexes which are compatible with lipids hence, enhancing the drug absorption and bioavailability. The technology tends to produce a small cell which can easily pass inside the cell and bloodstream in order to protect the important constituents of plant extract against digestive secretions and microorganisms. The carrier system provides advantages such as enhanced stability and bioavailability [12].

Qian et al. suggested in his study on silybin that, due to the improvised lipophilic property of the complex enhanced bioavailability has been observed in rats. However, Petyaev et al., developed a novel hesperetin through a combination with phosphatidyl choline which shows enhanced phytosomes bioavailability. Similarly, Lu et al., prepared and studied the oral bioavailability of rutin which was found to be enhanced in phytosomes (Figure 2).

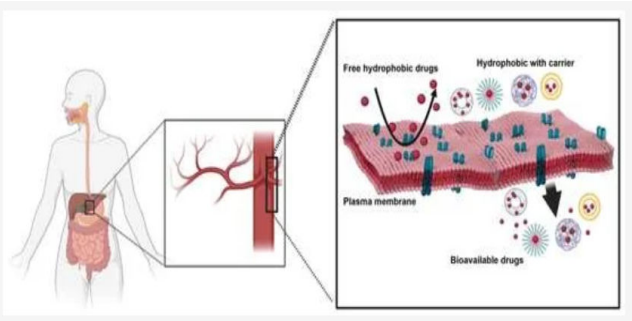

Figure 2: Enhanced bioavailability of drug through NDDS.

CONCLUSION

Drug bioavailability is an important factor which affects the drug development and its therapeutic efficacy. The review study suggested that the standard requirement to enhance the drug bioavailability is the rate of dissolution and its formulation solubility. Therefore, enhanced bioavailability enhancement of drugs with low solubility and permeability is considered as challenging aspects to develop drugs in terms of their formulations. In order to increase the rate of dissolution several conventional approaches are preferred such as reduced size of the particle, emulsification/self-emulsification, inclusions of cyclodextrin, etc. It has been observed that nano suspensions provided enhancement in the level of solubility, rate of dissolution and bioavailability of the drugs which are hydrophobic in nature. Similarly, SLN depicted increased drug oral bioavailability. Emulsified drug delivery systems such as nanoemulsions, SEDDS, etc., are also found to be helpful in enhancing the bioavailability both *in vitro* and *in vivo*. Therefore, it is concluded that a novel drug delivery systems are potential enough to enhance the bioavailability of drugs.

COMPETING INTEREST

The author declares that they have no competing interests.

FUNDING

No funding was required for the research paper.

AUTHORS CONTRIBUTION

The work has been completed by me in all aspects.

CONFLICT OF INTEREST

The authors of the review article titled 'new deliveries used to enhance bioavailability through novel drug delivery systems' has no conflict of interest to declare.

ACKNOWLEDGEMENT

I would like to thank god for bestowing his mercy upon me. I would like to also thank my parents and teachers for their kind guidance and support in every phase of my life.

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